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 NEWS  5  Apr 23  Search Derwent WPINDEX by chemical structure
 NEWS  6  Apr 23  PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
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=> s ACE inhibitor or angiotensin converting enzyme inhibitor

L1 53318 ACE INHIBITOR OR ANGIOTENSIN CONVERTING ENZYME INHIBITOR

=> s congestive heart failure or diabetes or stroke

L2 845983 CONGESTIVE HEART FAILURE OR DIABETES OR STROKE

=> s l1 and l2

L3 11384 L1 AND L2

=> s l3 and py<1998

2 FILES SEARCHED...
4 FILES SEARCHED...
L4 7148 L3 AND PY<1998

=> s l4 and diabetes and stroke and congestive heart failure

L5 48 L4 AND DIABETES AND STROKE AND CONGESTIVE HEART FAILURE

=> dup rem

ENTER L# LIST OR (END):l5

PROCESSING COMPLETED FOR L5
L6 41 DUP REM L5 (7 DUPLICATES REMOVED)

=> d l6 1-8 kwic bib ab

L6 ANSWER 1 OF 41 USPATFULL
PI US 6107329 20000822
WO 9639384 19961212 <--
AB . . . R.sub.9 or C(O)R.sub.12 as glucogen phosphorylase inhibitors, pharmaceutical compositions containing such inhibitors and the use of such inhibitors to treat **diabetes**, hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemia, hyperlipidemia, atherosclerosis and myocardial ischemia in mammals.
SUMM This invention relates to glycogen phosphorylase inhibitors, pharmaceutical compositions containing such inhibitors and the use of such inhibitors to treat **diabetes**, hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemia, hyperlipidemia, atherosclerosis and myocardial ischemia in mammals.
SUMM In spite of the early discovery of insulin and its subsequent widespread use in the treatment of **diabetes**, and the later discovery of and use of sulfonylureas (e.g. Chlorpropamide.TM. (Pfizer), Tolbutamide.TM. (Upjohn), Acetohexamide.TM. (E. I. Lilly), Tolazamide.TM. (Upjohn)) and biguanides (e.g. Phenformin.TM. (Ciba Geigy), Metformin.TM. (G. D. Searle)) as oral hypoglycemic agents, the treatment of **diabetes** remains less than satisfactory. The use of insulin, necessary in about 10% of diabetic patients in which synthetic hypoglycemic agents are not effective Type I **diabetes**, insulin dependent **diabetes** mellitus), requires multiple daily doses, usually by self injection. Determination of the proper dosage of insulin requires frequent estimations of. . . causes hypoglycemia, with effects ranging from mild abnormalities in blood glucose to coma, or even death. Treatment of non-insulin dependent **diabetes** mellitus (Type II **diabetes**, NIDDM) usually consists of a combination of diet, exercise, oral agents, e.g. sulfonylureas, and in more severe cases, insulin. However,. . .
SUMM . . . whom the causative agent or disorder is unknown. While such

"essential" hypertension is often associated with disorders such as obesity, **diabetes** and hypertriglyceridemia, the relationship between these disorders has not been elucidated. Additionally, many patients display the symptoms of high blood. . .

SUMM It is known that hypertension can directly lead to heart failure, renal failure and **stroke** (brain hemorrhaging). These conditions are capable of causing short-term death in a patient. Hypertension can also contribute to the development. . .

SUMM . . . treatment of essential hypertension has been undertaken bearing the foregoing factors in mind. Thus a broad range of beta-blockers, vasoconstrictors, **angiotensin converting enzyme inhibitors** and the like have been developed and marketed as antihypertensives. The treatment of hypertension utilizing these compounds has proven beneficial. . .

SUMM Cardiac hypertrophy is a significant risk factor in the development of sudden death, myocardial infarction, and **congestive heart failure**. These cardiac events are due, at least in part, to increased susceptibility to myocardial injury after ischemia and reperfusion which. . .

SUMM This invention is directed to a glycogen phosphorylase inhibitor compound of Formula I useful for the treatment of **diabetes**, hyperglycemia, hypercholesterolemia, hyperinsulinemia, hypertension, hyperlipidemia, atherosclerosis and myocardial ischemia.

SUMM Yet another aspect of this invention is directed to a method for treating **diabetes** in a mammal by administering to a mammal suffering from **diabetes** a **diabetes** treating amount of a Formula I compound. Included in the treatment of **diabetes** is the prevention or attenuation of long term complications such as neuropathy, nephropathy, retinopathy or cataracts.

SUMM Another aspect of this invention is directed to pharmaceutical compositions for the treatment of **diabetes** which comprise a therapeutically effective amount of a glycogen phosphorylase inhibitor;

SUMM Another aspect of this invention is a method of treating **diabetes** in a mammal with the above described combination compositions.

SUMM . . . glycogen molecule. These disorders are ameliorated by reduction of or characterized by an elevation of glycogen phosphorylase activity. Examples include **diabetes**, hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemia, hyperlipidemia, atherosclerosis and myocardial ischemia.

CLM What is claimed is:

36. The method as recited in claim 34 for treating **diabetes** in a mammal by administering to a mammal suffering from **diabetes** a **diabetes** treating amount of a compound of claim 1.

AN 2000:109834 USPATFULL|

TI Substituted n-(indole-2-carbonyl)-glycinamides and derivatives as glycogen phosphorylase inhibitors|

IN Hoover, Dennis J., Stonington, CT, United States
Hulin, Bernard, Essex, CT, United States
Martin, William H., Essex, CT, United States
Phillips, Douglas, Gales Ferry, CT, United States
Treadway, Judith L., Gales Ferry, CT, United States

PA Pfizer, Inc., New York, NY, United States (U.S. corporation)

PI US 6107329 20000822
WO 9639384 19961212 <--

AI US 1997-952669 19971202 (8)
WO 1995-IB442 19950606
19971202 PCT 371 date
19971202 PCT 102(e) date

DT Utility|

EXNAM Primary Examiner: Riley, Jezia|

LREP Richardson, Peter C.; Benson, Gregg C.; Olson, A. Dean|

CLMN Number of Claims: 44|
ECL Exemplary Claim: 1|
DRWN No Drawings
LN.CNT 5662|
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of Formula (1) wherein R.sub.6 is carboxy, (C.sub.1 -C.sub.8)alkoxycarbonyl, benzyloxycarbonyl, C(O)NR.sub.8 R.sub.9 or C(O)R.sub.12 as glucogen phosphorylase inhibitors, pharmaceutical compositions containing such inhibitors and the use of such inhibitors to treat **diabetes**, hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemia, hyperlipidemia, atherosclerosis and myocardial ischemia in mammals.

L6 ANSWER 2 OF 41 USPATFULL
PI US 6039978 20000321
WO 9639053 19961212 <--
SUMM . . . exists with respect to special diet situations, including those associated with diet-responsive conditions, such as cardiovascular disease (hypertension and hyperlipidemia), **diabetes** and cancer.
SUMM . . . excess weight. Excess weight is associated with an increased risk of several chronic disorders, including non-insulin dependent (or Type II) **diabetes**, hypertension, and cardiovascular disease, such as coronary heart disease (CHD) and atherosclerotic disease. These risks, however, appear to decline following. . .
SUMM Another diet-responsive condition which may be helped by improved health management is non-insulin dependent **diabetes**. Generally, the bodies of patients suffering from non-insulin dependent **diabetes** produces insulin, but the insulin produced does not function properly. Insulin dependent diabetics do not produce any insulin and must. . . insulin to avoid ketoacidosis, i.e., the build-up of ketones in the blood stream. Some non-insulin dependent diabetics may control their **diabetes** simply by limiting the amount and types of foods and beverages that they consume and increasing their physical activity levels. . .
SUMM The America **Diabetes** Association (ADA) states that non-insulin dependent diabetics may use a combination of diet, exercise, and medication to lower plasma glucose. . . maintain control over body weight. As noted above, obesity may be linked to the onset or progression of non-insulin dependent **diabetes**. Moreover, insulin functions better in persons near their appropriate body weight. Weight increases also may cause **diabetes**-related problems, such as hypertension or CHD. Therefore, an appropriate diet for diabetics generally is calculated to include management of caloric. . .
SUMM It also is increasingly appreciated that hypertension, non-insulin dependent **diabetes**, and various dyslipidemias frequently coexist. Further, these conditions may share common pathophysiological features including insulin resistance, hyperinsulinemia, and abnormal sodium. . .
SUMM . . . health management, i.e., preventing or treating and reducing risk factors associated with diet-responsive conditions, such as: obesity; hyperlipidemia; non-insulin dependent **diabetes**; hypertension; and cancer, for example, colo-rectal cancer; by supplying a diet providing recommended dietary levels of macro- and micronutrients. In. . .
SUMM . . . for administration to a patient having at least one diet-responsive condition. Such diet-responsive condition may include obesity, hypertension, hyperlipidemia, cancer, **diabetes**, and combinations thereof. The system may comprise a meal program containing a plurality of prepackaged individual meals. Each of these. . .
DETD . . . dietary system for a patient having at least one diet-responsive condition. Such diet-responsive conditions may include obesity, hypertension, hyperlipidemia, cancer, **diabetes**, and

combinations thereof. The system comprises a meal program containing a plurality of prepackaged individual meals. Each of the individual. . .

DETD . . . Research Council, Food and Nutrition Board Subcommittee on the Recommended Dietary Allowances) and scientific/professional organization (e.g., National Cancer Institute, American **Diabetes** Association, American Heart Association, and American Dietetic Association); (3) sodium in an amount less than about 3000 mg; (4) protein,. . .

DETD . . . the addition of potassium to a patient's diet has positive health effects. In epidemiologic and animal studies, the risk of **stroke**-related deaths has been shown to be inversely related to potassium intake. These results have been observed over a range of. . .

DETD . . . high potassium diet may result in lower blood pressure levels. Moreover, such a diet may result in reduced frequency of **stroke** .

DETD **Diabetes**

DETD The indicators associated with diet-responsive **diabetes** are determined for the individual patient. The diet is designed to control plasma glucose and plasma lipid levels and maintain. . .

DETD . . . (1) hypertension, e.g., meals with low sodium content; (2) hyperlipidemia, e.g., meals low in cholesterol and SFAs; (3) non-insulin dependent **diabetes**, e.g., low in simple sugars and high in fiber; (4) cancer prevention, e.g., high in fiber low in cholesterol and. . .

DETD . . . quantifiable treatment indicator usually will be body weight and Body Mass Index (BMI). Similarly, when the condition is non-insulin dependent **diabetes** mellitus, the quantifiable treatment indicators may be fasting plasma glucose level and HbA.sub.1c. When the condition is hyperlipidemia, the quantifiable. . .

DETD . . . Allowances and followed the dietary guidelines of the AHA for total fat, saturated fat, cholesterol, and sodium and the American **Diabetes** Association recommendations for reducing simple sugar intake.

DETD . . . four diagnostic categories: Category C.sub.1 : mild to moderate essential hypertension, Category C.sub.2 : hyperlipidemia: Category C.sub.3 : non-insulin treated **diabetes** mellitus; and Category C.sub.4 : two or all three of the above Categories C.sub.1 -C.sub.3. All subjects were required to. . .

DETD Category C.sub.3 --Non-insulin Dependent **Diabetes**. Either:

DETD 3. Myocardial infarction within about 6 months, angina pectoris, **congestive heart failure**, insulin treatment for **diabetes** or secondary forms of hypertension;

DETD TABLE XXVIII

DIET-RESPONSIVE CONDITION: HYPERTENSION

TREATMENT	REDUCTION (mmHg) SYSTOLIC	DIASTOLIC
PREPARED DIET	7.0	4.1
CONTROL DIET	3.7	3.2
ACE INHIBITORS	8	4
BETA-BLOCKERS	9	6
CALCIUM CHANNEL BLOCKERS	7	5
DIURETIC	11	5
PERIPHERAL ANTIADVERERGIC AGENT	5	4

DETD . . . Plasma glucose levels of diabetic patients using stabilizing medication experience stabilization or a trend toward reduction.

Patients who control their **diabetes** without medication generally experience a trend toward the reduction of plasma glucose levels.

AN 2000:34224 USPATFULL
TI Dietary food enhancement agent
IN Bangs, William E., Philadelphia, PA, United States
Khoo, Chor San Heng, Mt. Laurel, NJ, United States
Ko, Sandy, Abington, PA, United States
PA Campbell Soup Company, Camden, NJ, United States (U.S. corporation)
PI US 6039978 20000321
WO 9639053 19961212 <--
AI US 1996-716421 19960920 (8)
WO 1996-US10225 19960606
19960920 PCT 371 date
19960920 PCT 102(e) date
RLI Continuation-in-part of Ser. No. US 1995-471202, filed on 6 Jun 1995, now abandoned
DT Utility
EXNAM Primary Examiner: Mosher, Mary E.
LREP Baker & Botts, L.L.P.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1,3
DRWN 4 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 3160
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention is a dietary food enhancement agent for fortifying food products. The agent includes a premixed combination of Vitamin A, Vitamin B.sub.1, Vitamin B.sub.2, Vitamin B.sub.6, Vitamin B.sub.12, Vitamin C, Vitamin D, Vitamin E, Vitamin K, Biotin, Calcium, Copper, Folic Acid, Iodine, Iron, Magnesium, Manganese, Pantothenic Acid, Phosphorus, and Zinc. Further, calcium may be supplied by a combination of calcium citrate and dicalcium phosphate, the phosphorus is supplied by a combination of dicalcium phosphate and magnesium phosphate, and the magnesium is supplied by magnesium phosphate.

L6 ANSWER 3 OF 41 USPATFULL
PI US 5861401 19990119
WO 9526957 19951012 <--
SUMM . . . cytokines. Elevated endothelin levels have been found in a number of disease states in man including hypertension, pulmonary hypertension, pre-eclampsia, **congestive heart failure**, myocardial infarction, angina pectoris, acute and chronic renal failure, ischaemic **stroke**, subarachnoid haemorrhage, atherosclerosis, hypercholesterolaemia, cardiogenic and endotoxic shock, **diabetes** mellitus, Raynaud's disease, scleroderma, systemic sclerosis, Buerger's disease, rheumatoid arthritis, asthma, bronchitis, acute respiratory failure, liver cirrhosis, Crohn's disease, ulcerative. . .
SUMM . . . of the invention will thus be useful in the treatment of diseases or medical conditions such as hypertension, pulmonary hypertension, **congestive heart failure**, dyslipidaemia, atherosclerosis, restenosis, acute and chronic renal failure, ischaemic **stroke**, subarachnoid haemorrhage, intermittent claudication, critical limb ischaemia, asthma, and organ failure after general surgery or translantation. They may also be useful for the treatment of pre-eclampsia, premature labour, myocardial infarction, angina pectoris, dysrrhythmia, cardiogenic and endotoxin shock, **diabetes** mellitus, Raynaud's disease, scleroderma, Buerger's disease, systemic sclerosis, bronchitis, acute respiratory distress syndrome, liver cirrhosis, osteoporosis, Crohn's disease, ulcerative colitis,. . .
SUMM . . . to hereinabove, such as beta-adrenergic blocker (for example atenolol), a calcium channel blocker (for example nifedipine), an angiotensin converting enzyme (**ACE**) **inhibitor** (for

example lisinopril), a diuretic (for example furosemide or hydrochlorothiazide), an endothelin converting enzyme (ECE) inhibitor (for example phosphoramidon), a. . .

CLM What is claimed is:
10. A method for the treatment of **congestive heart failure** in a human or other warm-blooded animal requiring such treatment which comprises administering to said human or other warm-blooded animal. . .

AN 1999:7388 USPATFULL|
TI N-heterocyclyl sulphonamide derivatives and their use as endothelin antagonists|
IN Bradbury, Robert Hugh, Macclesfield, United Kingdom
PA Zeneca Limited, London, United Kingdom (non-U.S. corporation)
PI US 5861401 19990119
WO 9526957 19951012 <--
AI US 1996-716194 19960930 (8)
WO 1995-GB702 19950329
19960930 PCT 371 date
19960930 PCT 102(e) date
PRAI GB 1994-6437 19940331
GB 1994-21548 19941026
DT Utility|
EXNAM Primary Examiner: Shah, Mukund; Assistant Examiner: Ngo, Tamthom T.|
CLMN Number of Claims: 18|
ECL Exemplary Claim: 1|
DRWN No Drawings
LN.CNT 2334|
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns pharmaceutically useful N-heterocyclyl sulphonamide derivatives, their pharmaceutically acceptable salts, processes for their manufacture, their use for antagonising one or more actions of endothelin in a human or other warm-blooded animal, their use
in methods of treatment of diseases or medical conditions in which elevated or abnormal levels of endothelin play a significant causative role.

L6 ANSWER 4 OF 41 USPATFULL
PI US 5679545 19971021 <--
SUMM Current therapy for heart failure is primarily directed to using angiotensin-converting enzyme (**ACE**) **inhibitors** and diuretics. While prolonging survival in the setting of heart failure, **ACE inhibitors** appear to slow the progression towards end-stage heart failure, and substantial numbers of patients on **ACE inhibitors** have functional class III heart failure. Moreover, **ACE inhibitors** consistently appear unable to relieve symptoms in more than 60% of heart failure patients and reduce mortality of heart failure. . .
SUMM . . . activation of physiological or compensatory hypertrophy can be beneficial in the setting of heart failure. In fact, the effects of **ACE inhibitors** have been purported not only to unload the heart, but also to inhibit the pathological hypertrophic response that has been. . .
SUMM Not only is there a need for an improvement in the therapy of heart failure such as **congestive heart failure**, but there is also a need to offer effective treatment for neurological disorders. Neurotrophic factors such as insulin-like growth factors,.
.
. means for enhancing neuronal survival, for example, as a treatment for neurodegenerative diseases such as amyotrophic lateral sclerosis, Alzheimer's disease, **stroke**, epilepsy, Huntington's disease, Parkinson's disease, and peripheral neuropathy. It would be desirable to
provide an additional therapy for this purpose.
SUMM . . . object of the present invention to provide an improved therapy for the prevention and/or treatment of heart failure such as

congestive heart failure, particularly the promotion of physiological forms of hypertrophy or inhibition of pathological forms of hypertrophy, and for the prevention and/or. . .

DETD . . . disorders include all neurodegenerative diseases, such as peripheral neuropathies (motor and sensory), amyotrophic lateral sclerosis (ALS), Alzheimer's disease, Parkinson's disease, **stroke**, Huntington's disease, epilepsy, and ophthalmologic diseases such as those involving the retina, e.g., diabetic retinopathy, retinal dystrophy, and retinal degeneration. . .

DETD . . . the rate needed for the requirements of metabolizing tissues. Heart failure includes a wide range of disease states such as **congestive heart failure**, myocardial infarction, and tachyarrhythmia.

DETD As used herein, **"ACE inhibitor"** refers to angiotensin-converting enzyme inhibiting drugs which prevent the conversion of angiotensin I to angiotensin II. The **ACE inhibitors** may be beneficial in **congestive heart failure** by reducing systemic vascular resistance and relieving circulatory congestion. The **ACE inhibitors** include but are not limited to those designated by the trademarks Accupril.RTM. (quinapril), Altace.RTM. (ramipril), Capoten.RTM. (captopril), Lotensin.RTM. (benazepril) Monoopril.RTM. (fosinopril), Prinivil.RTM. (lisinopril), Vasotec.RTM. (enalapril), and Zestril.RTM. (lisinopril). One example of an **ACE inhibitor** is that sold under the trademark Capoten.RTM.. Generically referred to as captopril, this **ACE inhibitor** is designated chemically as 1-[(2S)-3-mercapto-2-methylpropionyl]-L-proline.

DETD . . . administering a therapeutically effective amount of a CMF to the mammal. Optionally, the CHF is administered in combination with an **ACE inhibitor**, such as captopril, in the case of **congestive heart failure**, or with another myocardiotrophic, anti-arrhythmic, or inotropic factor in the case of other types of heart failure or cardiac disorder,. . .

DETD For example, CHF may be useful in treating **congestive heart failure** in cases where **ACE inhibitors** cannot be employed or are not as effective. CHF optionally is combined with or administered in concert with other agents for treating **congestive heart failure**, including **ACE inhibitors**.

DETD The effective amount of **ACE inhibitor** to be administered, if employed, will be at the physician's or veterinarian's discretion. Dosage administration and adjustment is done to achieve optimal management of **congestive heart failure** and ideally takes into account use of diuretics or digitalis, and conditions such as hypotension and renal impairment. The dose. . . and the specific patient being treated. Typically the amount employed will be the same dose as that used if the **ACE inhibitor** were to be administered without CHF.

DETD . . . administration in tablet or capsule form. A discussion of the dosage, administration, indications and contraindications associated with captopril and other **ACE inhibitors** can be found in the Physicians Desk Reference, Medical Economics Data Production Co., Montvale, N.J. 2314-2320 (1994).

DETD . . . into the treatment of all neurodegenerative diseases by CHF, including peripheral neuropathies (motor and sensory), ALS, Alzheimer's disease, Parkinson's disease, **stroke**, Huntington's disease, and ophthalmologic diseases, for example, those involving the retina.

DETD . . . be one which increases ventricular contractility and decreases peripheral vascular resistance or ameliorates or treats conditions of similar importance in **congestive heart failure** patients. The progress of this therapy is easily monitored by conventional assays.

DETD . . . endothelin, neonatal rat myocardial cells in culture display several features of the in vivo cardiac muscle cell hypertrophy seen in **congestive heart failure**, including an increase in cell size and an increase in the assembly of an individual contractile protein into organized contractile. . .

DETD . . . heart beat, concentric or dilated hypertrophy, left ventricular systolic pressure, left ventricular mean pressure, left ventricular end-diastolic pressure, cardiac output, **stroke** index, histological parameters, ventricular size, wall thickness, etc.

DETD The purified CHF is also tested in a post-myocardial infarction rat model, which is predictive of human **congestive heart failure** in producing natriuretic peptide. Specifically, male Sprague-Dawley rats (Charles River Breeding Laboratories, Inc., eight weeks of age) are acclimated to. . .

DETD In clinical patients, myocardial infarction or coronary artery disease is the most common cause of heart failure. **Congestive heart failure** in this model reasonably mimics **congestive heart failure** in most human patients.

DETD . . . is monitored by VR-16 simultrace recorders (Honeywell Co., New York) and cardiac output (CO) is digitally obtained by the microcomputer. **Stroke** volume (SV)=CO/HR; Cardiac index (CI)=CO/BW; Systemic vascular resistance (SVR)=MAP/CI.

DETD . . . and ligated rat controls. This expected result would demonstrate that administration of CHF or CHF antagonist improves cardiac function in **congestive heart failure** . In sham rats, however, CHF or CHF antagonist administration at this dose is not expected to alter significantly cardiac function. . .

DETD . . . are determined at the time of re-evaluation, the dose would be adjusted upward. Concurrent medication doses (e.g., captopril as an **ACE inhibitor** and diuretics) would be adjusted at the discretion of the study physician. After the maximum dose is administered for 8. . .

DETD . . . or peak exercise VO.sub.2 <16 mL/kg/min. (adjusted for age), stable for at least one month on digoxin, diuretics, and vasodilators (**ACE inhibitors**).

DETD Concurrent **ACE inhibitor** therapy.

DETD **Diabetes** mellitus or impaired glucose tolerance.

AN 97:96744 USPATFULL

TI Gene encoding cardiac hypertrophy factor

IN Baker, Joffre, El Granada, CA, United States
Chien, Kenneth, La Jolla, CA, United States
King, Kathleen, Pacifica, CA, United States
Pennica, Diane, Burlingame, CA, United States
Wood, William, San Mateo, CA, United States

PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
The Regents of the University of California, Oakland, CA, United States (U.S. corporation)

PI US 5679545 19971021 <--

AI US 1995-443952 19950517 (8)

RLI Division of Ser. No. US 1994-286304, filed on 5 Aug 1994, now patented, Pat. No. US 5571893, issued on 5 Nov 1996 which is a continuation-in-part of Ser. No. US 1994-233609, filed on 25 Apr 1994, now patented, Pat. No. US 5534615, issued on 9 Jul 1996

DT Utility

EXNAM Primary Examiner: Arthur, Lisa B.

LREP Hasak, Janet E.; Torchia, Timothy E.; Conley, Deirdre L.

CLMN Number of Claims: 18

ECL Exemplary Claim: 1,8,9,10

DRWN 8 Drawing Figure(s); 8 Drawing Page(s)

LN.CNT 4217

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Isolated CT-1, isolated DNA encoding CT-1, and recombinant or synthetic methods of preparing CT-1 are disclosed. These CT-1 molecules are shown

to influence hypertrophic activity and neurological activity. Accordingly, these compounds or their antagonists may be used for treatment of heart failure, arrhythmic disorders, inotropic disorders, and neurological disorders.

L6 ANSWER 5 OF 41 USPATFULL
PI US 5668137 19970916 <--
SUMM . . . cytokines. Elevated endothelin levels have been found in a number of disease states in man including hypertension, pulmonary hypertension, pre-eclampsia, **congestive heart failure**, myocardial infarction, angina pectoris, acute and chronic renal failure, ischaemic **stroke**, subarachnoid haemorrhage, atherosclerosis, hypercholesterolaemia, cardiogenic and endotoxic shock, **diabetes** mellitus, Raynaud's disease, scleroderma, systemic sclerosis, Buerger's disease, rheumatoid arthritis, asthma, bronchitis, acute respiratory failure, liver cirrhosis, Crohn's disease, ulcerative. . .
SUMM . . . of the invention will thus be useful in the treatment of diseases or medical conditions such as hypertension, pulmonary hypertension, **congestive heart failure**, dyslipidaemia, atherosclerosis, restenosis, acute and chronic renal failure, ischaemic **stroke**, subarachnoid haemorrhage, intermittent claudication, critical limb ischaemia, asthma, and organ failure after general surgery or translantation. They may also be useful for the treatment of pre-eclampsia, premature labour, myocardial infarction, angina pectoris, dysrrhythmia, cardiogenic and endotoxin shock, **diabetes** mellitus, Raynaud's disease, scleroderma, Buerger's disease, systemic sclerosis, bronchitis, acute respiratory distress syndrome, liver cirrhosis, osteoporosis, Crohn's disease, ulcerative colitis,. . .
SUMM . . . to hereinabove, such as beta-adrenergic blocker (for example atenolol), a calcium channel blocker (for example nifedipine), an angiotensin converting enzyme (**ACE**) **inhibitor** (for example lisinopril), a diuretic (for example furosemide or hydrochlorothiazide), an endothelin converting enzyme (ECE) inhibitor (for example phosphoramidon), a. . .
AN 97:83963 USPATFULL
TI N-heterocyclic sulfonamides having endothelin receptor activity
IN Phillips, Paul John, Congleton, United Kingdom
Ballard, Peter Grahame, Stockport, United Kingdom
Bradbury, Robert Hugh, Wilmslow, United Kingdom
James, Roger, Congleton, United Kingdom
PA Zeneca Ltd., London, England (non-U.S. corporation)
PI US 5668137 19970916 <--
AI US 1996-667131 19960620 (8)
PRAI GB 1995-12697 19950622
DT Utility
EXNAM Primary Examiner: Grumbling, Matthew V.; Assistant Examiner: Bucknum, Michael
LREP Harris, Robert J.; Higgins, Patrick H.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1619
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns pharmaceutically useful compounds of the formula I, in which R.sup.1, R.sup.2, R.sup.3, n, m and Het have any of the meanings defined herein, and their pharmaceutically-acceptable salts, and pharmaceutical compositions containing them. The novel compounds possess endothelin receptor antagonist activity and are useful, for example, in the treatment of diseases or medical conditions in which elevated or abnormal levels of endothelin play a significant causative role. The invention further concerns processess for the manufacture of the novel compounds and the use of the compounds in medical treatment.

L6 ANSWER 6 OF 41 USPATFULL
TI Treatment of **congestive heart failure**
PI US 5661122 19970826 <--
AB Methods of enhancing myocardial contractility and cardiac performance in a mammal with **congestive heart failure** are disclosed. In a first method a mammal with **congestive heart failure** is treated by administering to the mammal an effective amount of a combination of growth hormone (GH) and insulin-like growth. . . comprises administering to the mammal an effective amount of a combination of GH and IGF-I in the presence of an **ACE inhibitor**. This method results in enhancement of myocardial contractility and cardiac performance above the level achieved with ACE inhibition alone. Preferably. . .
SUMM This invention relates to the field of treating patients having **congestive heart failure** with growth hormone and insulin-like growth factor I in the presence or absence of an angiotensin-converting enzyme (**ACE**) **inhibitor**.
SUMM . . . for two weeks improved cardiac function by increasing ventricular contractility and by decreasing peripheral vascular resistance in conscious rats with **congestive heart failure**. Yang, R. et al., Clinical Research 42(2):325A (1994).
SUMM . . . U. et at., Basic Res. Cardiol. 83:647-654 (1988). Acute intravenous administration (infusion or bolus injection) of IGF-I produces increases in **stroke** volume and cardiac output in normal lambs. Gluckman et al., PCT WO 92/11865 (1992). In rats with doxorubicin induced cardiomyopathy, chronic treatment with IGF-I for 3 weeks increases cardiac output and **stroke** volume. Ambler, G. R. et al., Cardiovascular Research 27:1368-1373 (1993).
SUMM Heart failure affects approximately three million Americans. New cases of heart failure number about 400,000 each year. **Congestive heart failure** is a syndrome characterized by left ventricular dysfunction, reduced exercise tolerance, impaired quality of life, and markedly shortened life expectancy.. . . cardiac output with consequent systemic arterial and venous vasoconstriction. This vasoconstriction, which promotes the vicious cycle of further reductions of **stroke** volume followed by an increased elevation of vascular resistance, appears to be mediated, in part, by the renin-angiotensis system. The. . . et al., N. England J. Med. 325(5):303-310 (1991); Captopril Multicenter Research Group, J. A. C. C. 2(4):755-763 (1983). Angiotensin-converting enzyme (**ACE**) **inhibitors**, such as captopril, have become standard therapy for patients with **congestive heart failure**. These drugs improve hemodynamic profile and exercise tolerance and reduce the incidence of morbidity and mortality in patients with **congestive heart failure**. Kramer, B. L. et al., Circulation 67(4):807-816 (1983); Captopril Multicenter Research Group, J. A. C. C. 2(4):755-763 (1983); The CONSENSUS. . . Engl. J. Med. 316(23):1429-1435 (1987); The SOLVD Investigators, N. Engl. J. Med. 325(5):293-302 (1991). However, despite proven efficacy, response to **ACE inhibitors** has been limited. Improvement of functional capacity and exercise time is only small and mortality, although reduced, continues to be. . .
SUMM Accordingly, it is an object of this invention to provide a method of treatment for patients with **congestive heart failure**, the method comprising administering to the patient GH and IGF-I in addition to an **ACE inhibitor**. It is well known, that captopril alone, for example, improves cardiac function by decreasing peripheral vascular resistance. Captopril together with. . .
SUMM It is another object of this invention to provide a method of treatment

for patients with **congestive heart failure**, the method comprising treating the patients with an effective amount of a combination of GH and IGF-I in the absence of an **ACE inhibitor**. The administration of GH and IGF-I in combination produces improvement of cardiac performance by increased ventricular contractility and decreased peripheral. . .

SUMM Improvement in cardiac performance for patients with **congestive heart failure** may be achieved in patients being treated with **ACE inhibitors** by adding to the treatment regimen a combination of GH and IGF-I. Improvement in cardiac performance in these patients may also be achieved by administration of GH/IGF-I and an **ACE inhibitor** from the outset of treatment.

SUMM The present invention achieves these objects by providing a method of treatment of **congestive heart failure**, the method characterized by administration of an effective amount of GH and IGF-I (GH/IGF-I) with or without an **ACE inhibitor**.

SUMM In one aspect, the present invention provides a method of treating a mammal exhibiting **congestive heart failure** comprising administering to the mammal an effective amount of a combination of GH and IGF-I and an **ACE inhibitor**. Administration of GH and IGF-I may be started after a period of treatment with the **ACE inhibitor**.

SUMM In another aspect, the invention provides a method of treating a mammal exhibiting **congestive heart failure** comprising administering to said mammal an effective amount of a combination of GH and IGF-I in the absence of an **ACE inhibitor**.

DRWD FIG. 6b shows the effect of GH/IGF-I (hatched bars) and vehicle alone (open bars) on **stroke** volume index (SVI) in water-treated and captopril-treated rats. *P<0.05, **P<0.01, compared to the respective vehicle group. ##P<0.01, compared to the. . .

DETD As used herein, "SV" refers to **stroke** volume. The **stroke** volume is measurable as CO/HR.

DETD As used herein, "SVI" refers to **stroke** volume index. The **stroke** volume index is measurable as SV/BW.

DETD As used herein "**congestive heart failure**" refers to a syndrome characterized by left ventricular dysfunction, reduced exercise tolerance, impaired quality of life, and markedly shortened life. . . vasoconstriction, which appears to be mediated, in part, by the renin-angiotensis system, promotes the vicious cycle of further reductions of **stroke** volume followed by an increased elevation of vascular resistance.

DETD As used herein "treatment" refers to induction of increased myocardial contractility and cardiac performance in patients experiencing **congestive heart failure**, as well as to prevention of **congestive heart failure**. Where the combination of GH and IGF-I is used in conjunction with an **ACE inhibitor**, the level of increased myocardial contractility and cardiac performance is increased above that resulting from use of the **ACE inhibitor** alone.

DETD As used herein, "**ACE inhibitor**" refers to angiotensin-converting enzyme inhibiting drugs which prevent the conversion of angiotensin I to angiotensin II. The **ACE inhibitors** may be beneficial in **congestive heart failure** by reducing systemic vascular resistance and relieving circulatory congestion. The **ACE inhibitors** include but are not limited to those designated by the trademarks Accupril.RTM. (quinapril), Altace.RTM. (ramipril), Capoten.RTM. (captopril), Lotensin.RTM. (benazepril), Monopril.RTM. (fosinopril), Prinivil.RTM. (lisinopril), Vasotec.RTM. (enalapril), and Zestril.RTM. (lisinopril). One example of an **ACE inhibitor** is that sold under the trademark Capoten.RTM.. Generically referred to as captopril, this **ACE inhibitor** is designated chemically as 1-[(2S)-3-mercapto-2-methylpropionyl]-L-proline.

DETD In the treatment of **congestive heart failure** by GH and IGF-I in combination, the GH and IGF-I compositions will be formulated, dosed, and administered in a fashion. . . thus determined by such considerations and are amounts that improve cardiac performance or ameliorate other conditions of similar importance in **congestive heart failure** patients.

DETD The effective amount of **ACE inhibitor** to be administered, if employed, will be at the physician's or veterinarian's discretion. Dosage administration and adjustment is done to achieve optimal management of **congestive heart failure** and ideally takes into account use of diuretics or digitalis, and conditions such as hypotension and renal impairment. The dose. . . and the specific patient being treated. Typically the amount employed will be the same dose as that used if the **ACE inhibitor** were to be administered without GH and IGF-I.

DETD . . . administration in tablet or capsule form. A discussion of the dosage, administration, indications and contraindications associated with captopril and other **ACE inhibitors** can be found in the Physicians Desk Reference, Medical Economics Data Production Co., Montvale, N.J. 2314-2320 (1994).

DETD Use of GH/IGF-I to Treat **Congestive Heart Failure** With and Without Prior and Concurrent Treatment With Captopril

DETD The goal of this study was to evaluate the cardiac effects of human GH/IGF-I in rats with **congestive heart failure** with and without prior and concurrent treatment with either captopril or water.

DETD . . . Animal Use" adopted Nov. 11, 1984 by the American Heart Association. After 4-6 weeks of ligation, myocardial infarction resulted in **congestive heart failure** in rats.

DETD . . . VR-16 simultrace recorders (Honeywell Co., N.Y.) and cardiac output (CO) was digitally obtained by the microcomputer. From the CO the **stroke** volume (SV), cardiac index (CI), **stroke** volume index (SVI), and systemic vascular resistance (SVR) can be calculated.

DETD Treatment for **congestive heart failure** with a combination of GH and IGF-I resulted in a significant increase in left ventricular maximum dP/dt, both in the. . .

DETD . . . decreases in arterial pressure, left ventricular end-diastolic pressure and peripheral vascular resistance. These changes resulted in increased cardiac output and **stroke** volume in the test animals. These are the well known benefits of ACE inhibition which are manifest in humans and. . .

DETD GH and IGF-I added to the treatment regimen of a mammal with **congestive heart failure** after an initial period of treatment with captopril induced effects of increased myocardial contractility and cardiac performance which were apparent.

. with captopril, GH, and IGF-I. The data suggest that captopril in combination with GH and IGF-I improves cardiac performance in **congestive heart failure.**

DETD These results suggest that after a period of treatment with captopril or other **ACE inhibitor**, a patient with **congestive heart failure** will benefit from addition of GH and IGF-I to the treatment regimen. These results also suggest that a patient will benefit from a combination of GH and IGF-I, even in the absence of an **ACE inhibitor.** Patients benefitting from a combination of GH and IGF-I in the absence of an **ACE inhibitor** are those for whom an **ACE inhibitor** is contraindicated and those who cannot tolerate the side effects of an **ACE inhibitor.**

DETD Proposed Clinical Treatment of **Congestive Heart Failure**

DETD Concurrent medication doses (diuretics and **ACE inhibitors**) would be adjusted at the discretion of the study physician. For example, a test dose of captopril is optionally given.

.

.

DETD . . . III or peak exercise VO.sub.2 .ltoreq.16 mL/kg/min. (adjusted for age), stable for at least one month on digoxin, diuretics, and **ACE inhibitors** (vasodilators).

DETD Concurrent **ACE inhibitor** therapy, in absence of noncardiac contraindication.

DETD **Diabetes** mellitus or impaired glucose tolerance.

CLM What is claimed is:

1. A method of treating **congestive heart failure** in a mammal who is not a GH-deficient adult, said method comprising administering to said mammal an effective amount of. . .

7. The method of claim 1 wherein the **congestive heart failure** results from acute or chronic ischemia.

8. The method of claim 1 wherein the **congestive heart failure** results from myocardial infarction.

AN 97:76104 USPATFULL|

TI Treatment of **congestive heart failure**|

IN Clark, Ross G., Pacifica, CA, United States
Jin, Hongkui, San Bruno, CA, United States
Paoni, Nicholas F., Belmont, CA, United States
Yang, Renhui, San Bruno, CA, United States

PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)

PI US 5661122 19970826 <--

AI US 1994-284859 19940802 (8)

RLI Continuation of Ser. No. US 1994-227923, filed on 15 Apr 1994, now abandoned

DT Utility|

EXNAM Primary Examiner: Jordan, Kimberly|

LREP Hasak, Janet E.; Dreger, Walter H.|

CLMN Number of Claims: 8|

ECL Exemplary Claim: 1|

DRWN 13 Drawing Figure(s); 6 Drawing Page(s)|

LN.CNT 1425|

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods of enhancing myocardial contractility and cardiac performance in a mammal with **congestive heart failure** are disclosed. In a first method a mammal with **congestive heart failure** is treated by administering to the mammal an effective amount of a combination of growth hormone (GH) and insulin-like growth factor (IGF-I). A second method comprises administering to the mammal an effective amount of a combination of GH and IGF-I in the presence of an **ACE inhibitor**. This method results in enhancement of myocardial contractility and cardiac performance above the level achieved with ACE inhibition alone. Preferably the mammal is a human.

L6 ANSWER 7 OF 41 USPATFULL

PI US 5641793 19970624 <--

SUMM . . . cytokines. Elevated endothelin levels have been found in a number of disease states in man including hypertension, pulmonary hypertension, pre-eclampsia, **congestive heart failure**, myocardial infarction, angina pectoris, acute and chronic renal failure, ischaemic **stroke**, subarachnoid haemorrhage, atherosclerosis, hypercholesterolaemia, cardiogenic and endotoxic shock, **diabetes** mellitus, Raynaud's disease, scleroderma, systemic sclerosis, Buerger's disease, rheumatoid

arthritis, asthma, bronchitis, acute respiratory failure, liver cirrhosis, Crohn's disease, ulcerative. . .

SUMM . . . of the invention will thus be useful in the treatment of diseases or medical conditions such as hypertension, pulmonary hypertension, **congestive heart failure**, dyslipidaemia, atherosclerosis, restenosis, acute and chronic renal failure, ischaemic **stroke**, subarachnoid haemorrhage, intermittent claudication, critical limb ischaemia, asthma, and organ failure after general surgery or translantation. They may also be useful for the treatment of pre-eclampsia, premature labour, myocardial infarction, angina pectoris, dysrrhythmia, cardiogenic and endotoxin shock, **diabetes** mellitus, Raynaud's disease, scleroderma, Buerger's disease, systemic sclerosis, bronchitis, acute respiratory distress syndrome, liver cirrhosis, osteoporosis, Crohn's disease, ulcerative colitis,. . .

SUMM . . . to hereinabove, such as beta-adrenergic blocker (for example atenolol), a calcium channel blocker (for example nifedipine), an angiotensin converting enzyme (**ACE**) **inhibitor** (for example lisinopril), a diuretic (for example furosemide or hydrochlorothiazide), an endothelin converting enzyme (ECE) inhibitor (for example phosphoramidon), a. . .

AN 97:54243 USPATFULL

TI Pyridine compounds which have useful pharmaceutical activity

IN Bradbury, Robert Hugh, Wilmslow, United Kingdom

PA Zeneca Limited, London, United Kingdom (non-U.S. corporation)

PI US 5641793 19970624 <--

AI US 1995-440133 19950512 (8)

PRAI GB 1994-9618 19940513

DT Utility

EXNAM Primary Examiner: Davis, Zinna Northington

LREP Harris, Robert J.

CLMN Number of Claims: 10

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1207

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention concerns pharmaceuticaly useful compounds of the formula I, in which Q, A.sup.1, A.sup.2, A.sup.3, R.sup.1, R.sup.2, R.sup.3 and R.sup.4 have any of the meanings defined herein, and their pharmaceutically acceptable salts, and pharmaceutically compositions containing them. The novel compounds possess endothelin receptor antagonist activity and are useful in the treatment of diseases or medical conditions in which elevated or abnormal levels of endothelin play a significant causative role. The invention further concerns processes for the manufacture of the novel compounds and the use of the compounds in medical treatment.

L6 ANSWER 8 OF 41 USPATFULL

PI US 5639471 19970617 <--

SUMM . . . exists with respect to special diet situations, including those associated with diet-responsive conditions, such as cardiovascular disease (hypertension and hyperlipidemia), **diabetes** and cancer.

SUMM . . . excess weight. Excess weight is associated with an increased risk of several chronic disorders, including non-insulin dependent (or Type lI) **diabetes**, hypertension, and cardiovascular disease, such as coronary heart disease (CHD) and atherosclerotic disease. These risks, however, appear to decline following. . .

SUMM Another diet-responsive condition which may be helped by improved health management is non-insulin dependent **diabetes**. Generally, the bodies of patients suffering from non-insulin dependent **diabetes** produce insulin, but the insulin produced does not function properly. Insulin dependent diabetics do not produce any insulin and must. . .

insulin to avoid ketoacidosis, i.e., the build-up of ketones in the blood stream. Some non-insulin dependent diabetics may control their **diabetes** simply by limiting the amount and types of foods and beverages that they consume and increasing their physical activity levels. . .

SUMM The America **Diabetes** Association (ADA) states that non-insulin dependent diabetics may use a combination of diet, exercise, and medication to lower plasma glucose. . . maintain control over body weight. As noted above, obesity may be linked to the onset or progression of non-insulin dependent **diabetes**. Moreover, insulin functions better in persons near their appropriate body weight. Weight increases also may cause **diabetes**-related problems, such as hypertension or CHD. Therefore, an appropriate diet for diabetics generally is calculated to include management of caloric. . .

SUMM It also is increasingly appreciated that hypertension, non-insulin dependent **diabetes**, and various dyslipidemias frequently coexist. Further, these conditions may share common pathophysiological features including insulin resistance, hyperinsulinemia, and abnormal sodium. . .

SUMM . . . health management, i.e., preventing or treating and reducing risk factors associated with diet-responsive conditions, such as: obesity; hyperlipidemia; non-insulin dependent **diabetes**; hypertension; and cancer, for example, colo-rectal cancer; by supplying a diet providing recommended dietary levels of macro- and micronutrients. In. . .

SUMM . . . for administration to a patient having at least one diet-responsive condition. Such diet-responsive condition may include obesity, hypertension, hyperlipidemia, cancer, **diabetes**, and combinations thereof. The system may comprise a meal program containing a plurality of prepackaged individual meals. Each of these. . .

DRWD . . . dietary system for a patient having at least one diet-responsive condition. Such diet-responsive conditions may include obesity, hypertension, hyperlipidemia, cancer, **diabetes**, and combinations thereof. The system comprises a meal program containing a plurality of prepackaged individual meals. Each of the individual. . .

DRWD . . . Research Council, Food and Nutrition Board Subcommittee on the Recommended Dietary Allowances) and scientific/professional organization (e.g., National Cancer Institute, American **Diabetes** Association, American Heart Association, and American Dietetic Association); (3) sodium in an mount less than about 3000 mg; (4) protein,. . .

DRWD . . . the addition of potassium to a patient's diet has positive health effects. In epidemiologic and animal studies, the risk of **stroke**-related deaths has been shown to be inversely related to potassium intake. These results have been observed over a range of. . .

DRWD . . . high potassium diet may result in lower blood pressure levels. Moreover, such a diet may result in reduced frequency of **stroke** .

DRWD **Diabetes**

DRWD The indicators associated with diet-responsive **diabetes** are determined for the individual patient. The diet is designed to control plasma glucose and plasma lipid levels and maintain. . .

DRWD . . . (1) hypertension, e.g., meals with low sodium content; (2) hyperlipidemia, e.g., meals low in cholesterol and SFAs; (3) non-insulin dependent **diabetes**, e.g., low in simple sugars and high in fiber; (4) cancer prevention, e.g., high in fiber low in cholesterol and. . .

DRWD . . . quantifiable treatment indicator usually will be body weight and Body Mass Index (BMI). Similarly, when the condition is non-insulin dependent **diabetes** mellitus, the quantifiable treatment indicators may be fasting plasma glucose level and HbA.sub.1c. When the

condition is hyperlipidemia, the quantifiable. . .

DETD . . . Allowances and followed the dietary guidelines of the AHA for total fat, saturated fat, cholesterol, and sodium and the American **Diabetes** Association recommendations for reducing simple sugar intake.

DETD . . . four diagnostic categories: Category C.sub.1 : mild to moderate essential hypertension; Category C.sub.2 : hyperlipidemia; Category C.sub.3 : non-insulin treated **diabetes** mellitus; and Category C.sub.4 : two or all three of the above Categories C.sub.1 -C.sub.3. All subjects were required to. . .

DETD CATEGORY C.sub.3 --Non-insulin Dependent **Diabetes**. Either:

DETD 3. Myocardial infarction within about 6 months, angina pectoris, **congestive heart failure**, insulin treatment for **diabetes** or secondary forms of hypertension;

DETD TABLE XXVIII

DIET-RESPONSIVE CONDITION: HYPERTENSION

TREATMENT	REDUCTION (mmHg) SYSTOLIC	DIASTOLIC
PREPARED DIET	7.0	4.1
CONTROL DIET	3.7	3.2
ACE INHIBITORS	8	4
BETA-BLOCKERS	9	6
CALCIUM CHANNEL BLOCKERS	7	5
DIURETIC	11	5
PERIEPHERAL ANTI-ADVERERGIC AGENT	5	4

DETD . . . Plasma glucose levels of diabetic patients using stabilizing medication experience stabilization or a trend toward reduction. Patients who control their **diabetes** without medication generally experience a trend toward the reduction of plasma glucose levels.

AN 97:51727 USPATFULL

TI Method for determining diet program effectiveness

IN Chait, Allen, Seattle, WA, United States
Hatton, Dan, Portland, OR, United States
Haynes, R. Brian, Dundas, Canada
Khoo, Chor San Heng, Mt. Laurel, NJ, United States
Kris-Etherton, Penny, State College, PA, United States
Macnair, R. David C., King of Prussia, PA, United States
McCarron, David, Portland, OR, United States
Metz, Jill, Portland, OR, United States
Oparil, Suzanne, Birmingham, AL, United States
Pi-Sunyer, Xavier, New York, NY, United States
Resnick, Larry, West Bloomfield, MI, United States
Stern, Judith S., Lafayette, CA, United States
Ziegler, Paula J., Cherry Hill, NJ, United States

PA Campbell Soup Company, Camden, NJ, United States (U.S. corporation)

PI US 5639471 19970617 <--

AI US 1995-469516 19950606 (8)

DT Utility

EXNAM Primary Examiner: Page, Thurman K.; Assistant Examiner: Shelborne, Kathryne E.

LREP Baker & Botts, L.L.P.

CLMN Number of Claims: 7

ECL Exemplary Claim: 1

DRWN 14 Drawing Figure(s); 8 Drawing Page(s)

LN.CNT 3163

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention is a method for determining the effectiveness of a diet

program for administration to a patient having at least one diet-responsive condition. The method includes the steps of selecting a plurality of patients, each having at least one diet-responsive condition; identifying at least one quantifiable indicator of each of the diet-responsive conditions and measuring the at least one indicator for each of the patient during a four week baseline period; and monitoring each of the patients during the baseline period to determine a baseline quality of life. The plurality of patient are divided randomly between a first group and a second group. The diet program is administered to each of the patients in the first group during a ten week intervention period and each of the patient in the second group is maintained on a control diet with known beneficial effects on the at least one diet-responsive condition during the intervention period. The at least one indicator of each of the conditions is monitored for each of the patient after the intervention period.

=> d 9-18 kwic bib

L6 ANSWER 9 OF 41 USPATFULL
PI US 5627073 19970506 <--
SUMM Current therapy for heart failure is primarily directed to using angiotensin-converting enzyme (**ACE**) **inhibitors** and diuretics. While prolonging survival in the setting of heart failure, **ACE inhibitors** appear to slow the progression towards end-stage heart failure, and substantial numbers of patients on **ACE inhibitors** have functional class III heart failure. Moreover, **ACE inhibitors** consistently appear unable to relieve symptoms in more than 60% of heart failure patients and reduce mortality of heart failure. . .
SUMM . . . activation of physiological or compensatory hypertrophy can be beneficial in the setting of heart failure. In fact, the effects of **ACE inhibitors** have been purported not only to unload the heart, but also to inhibit the pathological hypertrophic response that has been. . .
SUMM Not only is there a need for an improvement in the therapy of heart failure such as **congestive heart failure**, but there is also a need to offer effective treatment for neurological disorders. Neurotrophic factors such as insulin-like growth factors,.
.
. means for enhancing neuronal survival, for example, as a treatment for neurodegenerative diseases such as amyotrophic lateral sclerosis, Alzheimer's disease, **stroke**, epilepsy, Muntington's disease, Parkinson's disease, and peripheral neuropathy. It would be desirable to provide an additional therapy for this purpose.
SUMM . . . object of the present invention to provide an improved therapy for the prevention and/or treatment of heart failure such as **congestive heart failure**, particularly the promotion of physiological forms of hypertrophy or inhibition of pathological forms of hypertrophy, and for the prevention and/or. . .
DETD . . . disorders include all neurodegenerative diseases, such as peripheral neuropathies (motor and sensory), amyotrophic lateral sclerosis (ALS), Alzheimer's disease, Parkinson's disease, **stroke**, Huntington's disease, epilepsy, and ophthalmologic diseases such as those involving the retina, e.g., diabetic retinopathy, retinal dystrophy, and retinal degeneration. . .
DETD . . . the rate needed for the requirements of metabolizing tissues. Heart failure includes a wide range of disease states such as **congestive heart failure**, myocardial infarction, and tachyarrhythmia.
DETD As used herein, **"ACE inhibitor"** refers to angiotensinconverting enzyme inhibiting drugs which prevent the conversion of angiotensin I to angiotensin II. The **ACE**

inhibitors may be beneficial in **congestive heart failure** by reducing systemic vascular resistance and relieving circulatory congestion. The **ACE inhibitors** include but are not limited to those designated by the trademarks Accupril.RTM. (quinapril), Altace.RTM. (ramipril), Capoten.RTM. (captopril), Lorensin.RTM. (benazepril), Monopril.RTM. (fosinopril), Prinivil.RTM. (lisinopril), Vasotec.RTM. (enalapril), and Zestril.RTM. (lisinopril). One example of an **ACE inhibitor** is that sold under the trademark Capoten.RTM.. Generically referred to as captopril, this **ACE inhibitor** is designated chemically as 1-[(2S)-3-mercapto-2-methylpropionyl]-L-proline.

DETD . . . administering a therapeutically effective amount of a CHF to the mammal. Optionally, the CHF is administered in combination with an **ACE inhibitor**, such as captopril, in the case of **congestive heart failure**, or with another myocardiotrophic, anti-arrhythmic, or inotropic factor in the case of other types of heart failure or cardiac disorder,. . .

DETD For example, CHF may be useful in treating **congestive heart failure** in cases where **ACE inhibitors** cannot be employed or are not as effective. CHF optionally is combined with or administered in concert with other agents for treating **congestive heart failure**, including **ACE inhibitors**.

DETD The effective amount of **ACE inhibitor** to be administered, if employed, will be at the physician's or veterinarian's discretion. Dosage administration and adjustment is done to achieve optimal management of **congestive heart failure** and ideally takes into account use of diuretics or digitalis, and conditions such as hypotension and renal impairment. The dose. . . and the specific patient being treated. Typically the amount employed will be the same dose as that used if the **ACE inhibitor** were to be administered without CHF.

DETD . . . administration in tablet or capsule form. A discussion of the dosage, administration, indications and contraindications associated with captopril and other **ACE inhibitors** can be found in the Physicians Desk Reference, Medical Economics Data Production Co., Montvale, N.J. 2314-2320 (1994).

DETD . . . into the treatment of all neurodegenerative diseases by CHF, including peripheral neuropathies (motor and sensory), ALS, Alzheimer's disease, Parkinson's disease, **stroke**, Huntington's disease, and ophthalmologic diseases, for example, those involving the retina.

DETD . . . be one which increases ventricular contractility and decreases peripheral vascular resistance or ameliorates or treats conditions of similar importance in **congestive heart failure** patients. The progress of this therapy is easily monitored by conventional assays.

DETD . . . endothelin, neonatal rat myocardial cells in culture display several features of the in vivo cardiac muscle cell hypertrophy seen in **congestive heart failure**, including an increase in cell size and an increase in the assembly of an individual contractile protein into organized contractile. . .

DETD . . . heart beat, concentric or dilated hypertrophy, left ventricular systolic pressure, left ventricular mean pressure, left ventricular end-diastolic pressure, cardiac output, **stroke** index, histological parameters, ventricular size, wall thickness, etc.

DETD The purified CHF is also tested in a post-myocardial infarction rat model, which is predictive of human **congestive heart failure** in producing natriuretic peptide. Specifically, male Sprague-Dawley rats (Charles River Breeding Laboratories, Inc., eight weeks of age) are acclimated to. . .

DETD In clinical patients, myocardial infarction or coronary artery disease is the most common cause of heart failure. **Congestive**

heart failure in this model reasonably mimics **congestive heart failure** in most human patients.

DETD . . . curve is monitored by VR-16 simultrace recorders (Honeywell Co., N.Y.) and cardiac output (CO) is digitally obtained by the microcomputer. **Stroke** volume (SV)=CO/HR; Cardiac index (CI)=CO/BW; Systemic vascular resistance (SVR)=MAP/CI.

DETD . . . and ligated rat controls. This expected result would demonstrate that administration of CHF or CHF antagonist improves cardiac function in **congestive heart failure** . In sham rats, however, CHF or CHF antagonist administration at this dose is not expected to alter significantly cardiac function. . .

DETD . . . are determined at the time of reevaluation, the dose would be adjusted upward. Concurrent medication doses (e.g., captopril as an **ACE inhibitor** and diuretics) would be adjusted at the discretion of the study physician. After the maximum dose is administered for 8. . .

DETD . . . or peak exercise VO.sub.2 <16 mL/kg/min. (adjusted for age), stable for at least one month on digoxin, diuretics, and vasodilators (**ACE inhibitors**).

DETD --Concurrent **ACE inhibitor** therapy.

DETD --**Diabetes** mellitus or impaired glucose tolerance.

AN 97:38416 USPATFULL

TI Hybridomas producing antibodies to cardiac hypertrophy factor

IN Baker, Joffre, El Granada, CA, United States
Chien, Kenneth, La Jolla, CA, United States
King, Kathleen, Pacifica, CA, United States
Pennica, Diane, Burlingame, CA, United States
Wood, William, San Mateo, CA, United States

PA Genentech, Inc., United States (U.S. corporation)
The Regents of the University of California, United States (U.S. corporation)

PI US 5627073 19970506 <--

AI US 1995-443129 19950517 (8)

RLI Division of Ser. No. US 1994-286304, filed on 5 Aug 1994 which is a continuation-in-part of Ser. No. US 1994-233609, filed on 25 Apr 1994, now abandoned

DT Utility

EXNAM Primary Examiner: Nucker, Christine M.; Assistant Examiner: Reeves, Julie E.

LREP Torchia, Timothy E.; Hasak, Janet E.

CLMN Number of Claims: 18

ECL Exemplary Claim: 1

DRWN 8 Drawing Figure(s); 8 Drawing Page(s)

LN.CNT 4258

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 10 OF 41 USPATFULL

PI US 5624806 19970429 <--

SUMM Current therapy for heart failure is primarily directed to using angiotensin-converting enzyme (**ACE**) **inhibitors** and diuretics, while prolonging survival in the setting of heart failure, **ACE inhibitors** appear to slow the progression towards end-stage heart failure, and substantial numbers of patients on **ACE inhibitors** have functional class III heart failure. Moreover, **ACE inhibitors** consistently appear unable to relieve symptoms in more than 60% of heart failure patients and reduce mortality of heart failure. . .

SUMM . . . activation of physiological or compensatory hypertrophy can be beneficial in the setting of heart failure. In fact, the effects of **ACE inhibitors** have been purported not only to unload the heart, but also to inhibit the pathological hypertrophic response that has been. . .

SUMM Not only is there a need for an improvement in the therapy of heart failure such as **congestive heart failure**, but there is also a need to offer effective treatment for neurological

disorders. Neurotrophic factors such as insulin-like growth factors,. . . means for enhancing neuronal survival, for example, as a treatment for neurodegenerative diseases such as amyotrophic lateral sclerosis, Alzheimer's disease, **stroke**, epilepsy, Huntington's disease, Parkinson's disease, and peripheral neuropathy. It would be desirable to provide an additional therapy for this purpose.

SUMM . . . object of the present invention to provide an improved therapy for the prevention and/or treatment of heart failure such as **congestive heart failure**, particularly the promotion of physiological forms of hypertrophy or inhibition of pathological forms of hypertrophy, and for the prevention and/or. . .

DETD . . . disorders include all neurodegenerative diseases, such as peripheral neuropathies (motor and sensory), amyotrophic lateral sclerosis (ALS), Alzheimer's disease, Parkinson's disease, **stroke**, Huntington's disease, epilepsy, and ophthalmologic diseases such as those involving the retina, e.g., diabetic retinopathy, retinal dystrophy, and retinal degeneration. . .

DETD . . . the rate needed for the requirements of metabolizing tissues. Heart failure includes a wide range of disease states such as **congestive heart failure**, myocardial infarction, and tachyarrhythmia.

DETD As used herein, "**ACE inhibitor**" refers to angiotensin-converting enzyme inhibiting drugs which prevent the conversion of angiotensin I to angiotensin II. The **ACE inhibitors** may be beneficial in **congestive heart failure** by reducing systemic vascular resistance and relieving circulatory congestion. The **ACE inhibitors** include but are not limited to those designated by the trademarks Accupril.RTM. (quinapril), Altace.RTM. (ramipril), Capoten.RTM. (captopril), Lorensin.RTM. (benazepril), Monopril.RTM. (fosinopril), Prinivil.RTM. (lisinopril), Vasotec.RTM. (enalapril), and Zestril.RTM. (lisinopril). One example of an **ACE inhibitor** is that sold under the trademark Capoten.RTM.. Generically referred to as captopril, this **ACE inhibitor** is designated chemically as 1-[(2S)-3-mercapto-2-methylpropionyl]-L-proline.

DETD . . . administering a therapeutically effective amount of a CHF to the mammal. Optionally, the CHF is administered in combination with an **ACE inhibitor**, such as captopril, in the case of **congestive heart failure**, or with another myocardiotrophic, anti-arrhythmic, or inotropic factor in the case of other types of heart failure or cardiac disorder,. . .

DETD For example, CHF may be useful in treating **congestive heart failure** in cases where **ACE inhibitors** cannot be employed or are not as effective. CHF optionally is combined with or administered in concert with other agents for treating **congestive heart failure**, including **ACE inhibitors**.

DETD The effective amount of **ACE inhibitor** to be administered, if employed, will be at the physician's or veterinarian's discretion. Dosage administration and adjustment is done to achieve optimal management of **congestive heart failure** and ideally takes into account use of diuretics or digitalis, and conditions such as hypotension and renal impairment. The dose. . . and the specific patient being treated. Typically the amount employed will be the same dose as that used if the **ACE inhibitor** were to be administered without CHF.

DETD . . . administration in tablet or capsule form. A discussion of the dosage, administration, indications and contraindications associated with captopril and other **ACE inhibitors** can be found in the Physicians Desk Reference, Medical Economics Data Production Co.,

Montvale, N.J. 2314-2320 (1994).

DETD . . . into the treatment of all neurodegenerative diseases by CHF, including peripheral neuropathies (motor and sensory), ALS, Alzheimer's disease, Parkinson's disease, **stroke**, Huntington's disease, and ophthalmologic diseases, for example, those involving the retina.

DETD . . . be one which increases ventricular contractility and decreases peripheral vascular resistance or ameliorates or treats conditions of similar importance in **congestive heart failure** patients. The progress of this therapy is easily monitored by conventional assays.

DETD . . . endothelin, neonatal rat myocardial cells in culture display several features of the in vivo cardiac muscle cell hypertrophy seen in **congestive heart failure**, including an increase in cell size and an increase in the assembly of an individual contractile protein into organized contractile. . .

DETD . . . heart beat, concentric or dilated hypertrophy, left ventricular systolic pressure, left ventricular mean pressure, left ventricular end-diastolic pressure, cardiac output, **stroke** index, histological parameters, ventricular size, wall thickness, etc.

DETD The purified CHF is also tested in a post-myocardial infarction rat model, which is predictive of human **congestive heart failure** in producing natriuretic peptide. Specifically, male Sprague-Dawley rats (Charles River Breeding Laboratories, Inc., eight weeks of age) are acclimated to. . .

DETD In clinical patients, myocardial infarction or coronary-artery disease is the most common cause of heart failure. **Congestive heart failure** in this model reasonably mimics **congestive heart failure** in most human patients.

DETD . . . is monitored by VR-16 simultrace recorders (Honeywell Co., New York) and cardiac output (CO) is digitally obtained by the microcomputer. **Stroke** volume (SV)=CO/HR; Cardiac index (CI)=CO/BW; Systemic vascular resistance (SVR)=MAP/CI.

DETD . . . and ligated rat controls. This expected result would demonstrate that administration of CHF or CHF antagonist improves cardiac function in **congestive heart failure** . In sham rats, however, CHF or CHF antagonist administration at this dose is not expected to alter significantly cardiac function. . .

DETD . . . are determined at the time of re-evaluation, the dose would be adjusted upward. Concurrent medication doses (e.g., captopril as an **ACE inhibitor** and diuretics) would be adjusted at the discretion of the study physician. After the maximum dose is administered for 8. . .

DETD . . . or peak exercise VO.sub.2 <16 mL/kg/min. (adjusted for age), stable for at least one month on digoxin, diuretics, and vasodilators (**ACE inhibitors**).

DETD Concurrent **ACE inhibitor** therapy.

DETD **Diabetes** mellitus or impaired glucose tolerance.

AN 97:36067 USPATFULL

TI Antibodies to cardiac hypertrophy factor and uses thereof

IN Baker, Joffre, El Granada, CA, United States
Chien, Kenneth, La Jolla, CA, United States
King, Kathleen, Pacifica, CA, United States
Pennica, Diane, Burlingame, CA, United States
Wood, William, San Mateo, CA, United States

PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
The Regents of the University of California, Oakland, CA, United States (U.S. corporation)

PI US 5624806 19970429 <--

AI US 1995-442745 19950517 (8)

RLI Division of Ser. No. US 1994-286304, filed on 5 Aug 1994 which is a continuation of Ser. No. US 1994-233609, filed on 25 Apr 1994, now patented, Pat. No. US 5534615

DT Utility

EXNAM Primary Examiner: Knode, Marian C.; Assistant Examiner: Johnson, Nancy A.
LREP Hasak, Janet E.; Torchia, Timothy E.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 8 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 4254
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 11 OF 41 USPATFULL
PI US 5612359 19970318 <--
SUMM . . . secondary to heart failure, radiation and chemotherapeutic injury, or other trauma; treatment of central nervous system vascular disorders, such as **stroke**, migraine and subarachnoid hemorrhage; treatment of central nervous system behavioral disorders; treatment of gastrointestinal diseases such as ulcerative colitis, Crohn's. . . regulation of cell growth; treatment of benign prostatic hypertrophy; restenosis following angioplasty or following any procedures including transplantation; therapy for **congestive heart failure** including inhibition of fibrosis; inhibition of left ventricular dilatation, remodeling and dysfunction; and treatment of hepatotoxicity and sudden death. The. . . The compounds of this invention may be useful in therapy for metabolic and neurological disorders; cancer; insulin-dependent and non insulin-dependent **diabetes** mellitus; neuropathy; retinopathy; maternal respiratory distress syndrome; dysmenorrhea; epilepsy; hemorrhagic and ischemic **stroke**; bone remodeling; psoriasis; and chronic inflammatory diseases such as rheumatoid arthritis, osteoarthritis, sarcoidosis and eczematous dermatitis (all types of dermatitis).
SUMM . . . as modulators of PDGF activity; platelet activating factor (PAF) antagonists; angiotensin II (AII) receptor antagonists; renin inhibitors; angiotensin converting enzyme (**ACE**) **inhibitors** such as captopril, zofenopril, fosinopril, ceranapril, alacepril, enalapril, delapril, pentopril, quinapril, ramipril, lisinopril and salts of such compounds; neutral endopeptidase (NEP) inhibitors; dual NEP-**ACE inhibitors**; HMG CoA reductase inhibitors such as pravastatin and mevacor; squalene synthetase inhibitors; bile acid sequestrants such as questran; calcium channel. . .
CLM What is claimed is:
30. A method of treating **congestive heart failure**, which comprises administering an effective **congestive heart failure** treating amount of a compound of claim 1.

34. A method of treating **congestive heart failure**, which comprises administering an effective **congestive heart failure** treating amount of a compound of claim 31.

38. A method of treating **congestive heart failure**, which comprises administering an effective **congestive heart failure** treating amount of a compound of claim 35.

42. A method of treating **congestive heart failure**, which comprises administering an effective **congestive heart failure** treating amount of a compound of claim 39.

46. A method of treating **congestive heart failure**, which comprises administering an effective **congestive heart failure** treating amount of a compound of claim 43.

50. A method of treating **congestive heart failure**, which comprises administering an effective **congestive heart failure** treating amount of a compound of claim 47.

54. A method of treating **congestive heart failure**, which comprises administering an effective **congestive heart failure** treating amount of a compound of claim 51.

58. A method of treating **congestive heart failure**, which comprises administering an effective **congestive heart failure** treating amount of a compound of claim 55.

62. A method of treating **congestive heart failure**, which comprises administering an effective **congestive heart failure** treating amount of a compound of claim 59.

66. A method of treating **congestive heart failure**, which comprises administering an effective **congestive heart failure** treating amount of a compound of claim 63.

70. A method of treating **congestive heart failure**, which comprises administering an effective **congestive heart failure** treating amount of a compound of claim 67.

. . . claim 1 is used in combination with at least one angiotensin II (AII) receptor antagonist, renin inhibitor, angiotensin converting enzyme (**ACE**) **inhibitor**, or dual neutral endopeptidase (NEP)-**ACE inhibitor**.

. . . pharmaceutical composition of claim 72, further comprising at least one angiotensin II (AII) receptor antagonist, renin inhibitor, angiotensin converting enzyme (**ACE**) **inhibitor**, or dual neutral endopeptidase (NEP)-**ACE inhibitor**.

AN 97:22802 USPATFULL|
TI Substituted biphenyl isoxazole sulfonamides|
IN Murugesan, Natesan, Lawrenceville, NJ, United States
PA Bristol-Myers Squibb Company, Princeton, NJ, United States (U.S. corporation)
PI US 5612359 19970318 <--
AI US 1995-487358 19950607 (8)
RLI Continuation-in-part of Ser. No. US 1995-368285, filed on 4 Jan 1995, now abandoned which is a continuation-in-part of Ser. No. US 1994-297187, filed on 26 Aug 1994, now abandoned
DT Utility|
EXNAM Primary Examiner: Gerstl, Robert|
LREP Babajko, Suzanne E.|
CLMN Number of Claims: 73|
ECL Exemplary Claim: 1|
DRWN No Drawings
LN.CNT 2316|
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 12 OF 41 USPATFULL
TI Treatment of **congestive heart failure**
PI US 5610134 19970311 <--
AB Methods of enhancing myocardial contractility and cardiac performance in

a mammal with **congestive heart failure** are disclosed. In a first method a mammal with **congestive heart failure** is treated by administering to the mammal an effective amount of a combination of growth hormone (GH) and insulin-like growth. . . comprises administering to the mammal an effective amount of a combination of GH and IGF-I in the presence of an **ACE inhibitor**. This method results in enhancement of myocardial contractility and cardiac performance above the level achieved with ACE inhibition alone. Preferably. . .

SUMM This invention relates to the field of treating patients having **congestive heart failure** with growth hormone and insulin-like growth factor I in the presence or absence of an angiotensin-converting enzyme (**ACE**) **inhibitor**.

SUMM . . . for two weeks improved cardiac function by increasing ventricular contractility and by decreasing peripheral vascular resistance in conscious rats with **congestive heart failure**. Yang, R. et al., Clinical Research 42(2):325A (1994).

SUMM . . . U. et al., Basic Res. Cardiol. 83:647-654 (1988). Acute intravenous administration (infusion or bolus injection) of IGF-I produces increases in **stroke** volume and cardiac output in normal lambs. Gluckman et al., PCT WO 92/11865 (1992). In rats with doxorubicin induced cardiomyopathy, chronic treatment with IGF-I for 3 weeks increases cardiac output and **stroke** volume. Ambler, G. R. et al., Cardiovascular Research 27:1368-1373 (1993).

SUMM Heart failure affects approximately three million Americans. New cases of heart failure number about 400,000 each year. **Congestive heart failure** is a syndrome characterized by left ventricular dysfunction, reduced exercise tolerance, impaired quality of life, and markedly shortened life expectancy.. . . cardiac output with consequent systemic arterial and venous vasoconstriction. This vasoconstriction, which promotes the vicious cycle of further reductions of **stroke** volume followed by an increased elevation of vascular resistance, appears to be mediated, in part, by the renin-angiotensis system. The. . . Cohn, J. N. et al., N. England J. Med. 325(5):303-310 (1991); Captopril Multicenter Research Group, J.A.C.C. 2(4):755-763 (1983). Angiotensin-converting enzyme (**ACE**) **inhibitors**, such as captopril, have become standard therapy for patients with **congestive heart failure**. These drugs improve hemodynamic profile and exercise tolerance and reduce the incidence of morbidity and mortality in patients with **congestive heart failure**. Kramer, B. L. et al., Circulation 67(4):807-816 (1983); Captopril Multicenter Research Group, J.A.C.C. 2(4):755-763 (1983); The CONSENSUS Trial Study Group,. . . Engl. J. Med. 316(23):1429-1435 (1987); The SOLVD Investigators, N. Engl. J. Med. 325(5):293-302 (1991). However, despite proven efficacy, response to **ACE inhibitors** has been limited. Improvement of functional capacity and exercise time is only small and mortality, although reduced, continues to be. . .

SUMM Accordingly, it is an object of this invention to provide a method of treatment for patients with **congestive heart failure**, the method comprising administering to the patient GH and IGF-I in addition to an **ACE inhibitor**. It is well known, that captopril alone, for example, improves cardiac function by decreasing peripheral vascular resistance. Captopril together with. . .

SUMM It is another object of this invention to provide a method of treatment for patients with **congestive heart failure**, the method comprising treating the patients with an effective amount of a combination of GH and IGF-I in the absence of an **ACE inhibitor**. The administration of GH and IGF-I in combination produces improvement of cardiac performance by increased ventricular contractility and decreased peripheral. . .

SUMM Improvement in cardiac performance for patients with **congestive**

heart failure may be achieved in patients being treated with **ACE inhibitors** by adding to the treatment regimen a combination of GH and IGF-I. Improvement in cardiac performance in these patients may also be achieved by administration of GH/IGF-I and an **ACE inhibitor** from the outset of treatment.

SUMM The present invention achieves these objects by providing a method of treatment of **congestive heart failure**, the method characterized by administration of an effective amount of GH and IGF-I (GH/IGF-I) with or without an **ACE inhibitor**.

SUMM In one aspect, the present invention provides a method of treating a mammal exhibiting **congestive heart failure** comprising administering to the mammal an effective amount of a combination of GH and IGF-I and an **ACE inhibitor**. Administration of GH and IGF-I may be started after a period of treatment with the **ACE inhibitor**.

SUMM In another aspect, the invention provides a method of treating a mammal exhibiting **congestive heart failure** comprising administering to said mammal an effective amount of a combination of GH and IGF-I in the absence of an **ACE inhibitor**.

DRWD FIG. 6b shows the effect of GH/IGF-I (hatched bars) and vehicle alone (open bars) on **stroke** volume index (SVI) in water-treated and captopril-treated rats. * P<0.05, ** P<0.01, compared to the respective vehicle group. ##P<0.01, compared. . .

DETD As used herein, "SV" refers to **stroke** volume. The **stroke** volume is measurable as CO/HR.

DETD As used herein, "SVI" refers to **stroke** volume index. The **stroke** volume index is measurable as SV/BW.

DETD As used herein **"congestive heart failure"** refers to a syndrome characterized by left ventricular dysfunction, reduced exercise tolerance, impaired quality of life, and markedly shortened life. . . vasoconstriction, which appears to be mediated, in part, by the renin-angiotensis system, promotes the vicious cycle of further reductions of **stroke** volume followed by an increased elevation of vascular resistance.

DETD As used herein "treatment" refers to induction of increased myocardial contractility and cardiac performance in patients experiencing **congestive heart failure**, as well as to prevention of **congestive heart failure**. Where the combination of GH and IGF-I is used in conjunction with an **ACE inhibitor**, the level of increased myocardial contractility and cardiac performance is increased above that resulting from use of the **ACE inhibitor** alone.

DETD As used herein, **"ACE inhibitor"** refers to angiotensin-converting enzyme inhibiting drugs which prevent the conversion of angiotensin I to angiotensin II. The **ACE inhibitors** may be beneficial in **congestive heart failure** by reducing systemic vascular resistance and relieving circulatory congestion. The **ACE inhibitors** include but are not limited to those designated by the trademarks Accupril.RTM. (quinapril), Altace.RTM. (ramipril), Capoten.RTM. (captopril), Lotensin.RTM. (benazepril), Monopril.RTM. (fosinopril), Prinivil.RTM. (lisinopril), Vasotec.RTM. (enalapril), and Zestril.RTM. (lisinopril). One example of an **ACE inhibitor** is that sold under the trademark Capoten.RTM.. Generically referred to as captopril, this **ACE inhibitor** is designated chemically as 1-[(2S)-3-mercapto-2-methylpropionyl]-L-proline.

DETD In the treatment of **congestive heart failure** by GH and IGF-I in combination, the GH and IGF-I compositions will be formulated, dosed, and administered in a fashion. . . thus determined by such considerations and are amounts that improve cardiac performance or ameliorate other conditions of similar importance in **congestive heart failure** patients.

DETD The effective amount of **ACE inhibitor** to be administered, if employed, will be at the physician's or veterinarian's discretion. Dosage administration and adjustment is done to achieve optimal management of **congestive heart failure** and ideally takes into account use of diuretics or digitalis, and conditions such as hypotension and renal impairment. The dose. . . . and the specific patient being treated. Typically the amount employed will be the same dose as that used if the **ACE inhibitor** were to be administered without GH and IGF-I.

DETD . . . administration in tablet or capsule form. A discussion of the dosage, administration, indications and contraindications associated with captopril and other **ACE inhibitors** can be found in the Physicians Desk Reference, Medical Economics Data Production Co., Montvale, N.J. 2314-2320 (1994).

DETD Use of GH/IGF-I to treat **Congestive Heart Failure** With and Without

DETD The goal of this study was to evaluate the cardiac effects of human GH/IGF-I in rats with **congestive heart failure** with and without prior and concurrent treatment with either captopril or water

DETD . . . Animal Use" adopted Nov. 11, 1984 by the American Heart Association. After 4-6 weeks of ligation, myocardial infarction resulted in **congestive heart failure** in rats.

DETD . . . VR-16 simultrace recorders (Honeywell Co., N.Y.) and cardiac output (CO) was digitally obtained by the microcomputer. From the CO the **stroke** volume (SV), cardiac index (CI), **stroke** volume index (SVI), and systemic vascular resistance (SVR) can be calculated.

DETD Treatment for **congestive heart failure** with a combination of GH and IGF-I resulted in a significant increase in left ventricular maximum dP/dt, both in the. . .

DETD . . . decreases in arterial pressure, left ventricular end-diastolic pressure and peripheral vascular resistance. These changes resulted in increased cardiac output and **stroke** volume in the test animals. These are the well known benefits of ACE inhibition which are manifest in humans and. . .

DETD GH and IGF-I added to the treatment regimen of a mammal with **congestive heart failure** after an initial period of treatment with captopril induced effects of increased myocardial contractility and cardiac performance which were apparent.

. with captopril, GH, and IGF-I. The data suggest that captopril in combination with GH and IGF-I improves cardiac performance in **congestive heart failure.**

DETD These results suggest that after a period of treatment with captopril or other **ACE inhibitor,** a patient with **congestive heart failure** will benefit from addition of GH and IGF-I to the treatment regimen. These results also suggest that a patient will benefit from a combination of GH and IGF-I, even in the absence of an **ACE inhibitor.** Patients benefitting from a combination of GH and IGF-I in the absence of an **ACE inhibitor** are those for whom an **ACE inhibitor** is contraindicated and those who cannot tolerate the side effects of an **ACE inhibitor.**

DETD Proposed Clinical Treatment of **Congestive Heart Failure**

DETD **Diabetes** mellitus or impaired glucose tolerance.

CLM What is claimed is:

1. A method of treating **congestive heart failure** in a mammal, said method comprising administering to said mammal an effective amount of a combination of GH, IGF-1, and an **ACE inhibitor.**

. . . The method of claim 1 wherein administration of GH and IGF-I is begun

following a period of treatment with the **ACE inhibitor** alone.

3. The method of claim 1 wherein the GH, IGF-I, and **ACE inhibitor** are administered together from the outset of treatment.

4. The method of claim 1 wherein the **ACE inhibitor** is captopril.

9. The method of claim 1 wherein the **congestive heart failure** results from acute or chronic ischemia.

10. The method of claim 1 wherein the **congestive heart failure** results from myocardial infarction.

AN 97:20504 USPATFULL|
TI Treatment of **congestive heart failure**|
IN Clark, Ross G., Pacifica, CA, United States
Jin, Hongkui, San Bruno, CA, United States
Paoni, Nicholas F., Belmont, CA, United States
Yang, Renhui, San Bruno, CA, United States
PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
PI US 5610134 19970311 <--
AI US 1994-333909 19941103 (8)
RLI Continuation of Ser. No. US 1994-284859, filed on 2 Aug 1994 which is a continuation of Ser. No. US 1994-227923, filed on 15 Apr 1994, now abandoned
DT Utility|
EXNAM Primary Examiner: Jordan, Kimberly|
LREP Hasak, Janet E.; Dreger, Walter H.|
CLMN Number of Claims: 10|
ECL Exemplary Claim: 1|
DRWN 13 Drawing Figure(s); 6 Drawing Page(s)|
LN.CNT 1257|
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 13 OF 41 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 1
TI **Angiotensin-converting enzyme inhibitors**, angiotensin II receptor antagonists and calcium channel blocking agents: A review of potential benefits and possible adverse reactions.
SO Journal of the American College of Cardiology, (1997) 29/7 (1414-1421).
Refs: 46
ISSN: 0735-1097 CODEN: JACCDI
AB A review of recent studies suggests that the use of angiotensin-converting enzyme (**ACE**) **inhibitors** may be preferred (usually along with a diuretic drug) as initial therapy in several subsets of hypertensive patients (i.e., those with **diabetes** and nephropathy or with diminished left ventricular function with or without symptoms of heart failure). Limited long-term data are available. . . reduce reinfarction in patients with ischemic heart disease (however, mortality is nut reduced). Long-acting formulas of CCBs appear to decrease **congestive heart failure** in patients with dilated, but not ischemic, cardiomyopathy and to decrease **strokes** and arrhythmias in hypertensive subjects. Short-acting agents (primarily those that increase heart rate) may increase coronary heart disease events in. . .
CT Medical Descriptors:

*atherosclerosis: . . . therapy
*ischemic heart disease: DT, drug therapy
*ischemic heart disease: DI, diagnosis
clinical feature
congestive cardiomyopathy
disease association
heart arrhythmia
heart failure
heart left ventricle function
human
kidney disease
medical research
morbidity
mortality
priority journal
review
stroke
*angiotensin receptor antagonist: CB, drug combination
*angiotensin receptor antagonist: DT, drug therapy
*calcium channel blocking agent: CB, drug combination
*calcium channel blocking agent:. . .

AN 97193456 EMBASE
DN 1997193456
TI **Angiotensin-converting enzyme inhibitors**, angiotensin II receptor antagonists and calcium channel blocking agents: A review of potential benefits and possible adverse reactions.
AU Moser M.
CS Dr. M. Moser, 13 Murray Hill Road, Scarsdale, NY 10583, United States
SO Journal of the American College of Cardiology, (1997) 29/7 (1414-1421).
Refs: 46
ISSN: 0735-1097 CODEN: JACCDI
PUI S 0735-1097(97)00096-X
CY United States
DT Journal; General Review
FS 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LA English
SL English

L6 ANSWER 14 OF 41 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
TI Antihypertensive therapy: **Angiotensin-converting enzyme inhibitors**, angiotensin II receptor antagonists, and calcium antagonists.
SO Medical Clinics of North America, (1997) 81/6 (1319-1333).
Refs: 61
ISSN: 0025-7125 CODEN: MCNAA
AB . . . preventing cardiovascular morbidity and mortality for a broad spectrum of hypertensive patients. ACEIs are particularly indicated for managing patients with **congestive heart failure** due to systolic dysfunction and patients with diabetic nephropathy, especially in Type I **diabetes**. Theoretically, the AII receptor antagonists will be equally effective for these indications, and randomized trials are now underway to demonstrate. . .
CT Medical Descriptors:
*antihypertensive . . . contraindication
drug induced disease: SI, side effect
drug mechanism
heart left ventricle hypertrophy
human
kidney function
major clinical study
meta analysis
practice guideline
priority journal

renin angiotensin aldosterone system
review
single blind procedure
stroke: PC, prevention
stroke: CO, complication
sublingual drug administration
sustained release preparation
treatment indication
*angiotensin receptor antagonist: PD, pharmacology
*angiotensin receptor antagonist: CT, clinical trial
*angiotensin receptor antagonist: DT,. . .

AN 97336877 EMBASE
DN 1997336877
TI Antihypertensive therapy: **Angiotensin-converting enzyme inhibitors**, angiotensin II receptor antagonists, and calcium antagonists.
AU Gifford R.W. Jr.
CS Dr. R.W. Gifford Jr., Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44105, United States
SO Medical Clinics of North America, (1997) 81/6 (1319-1333).
Refs: 61
ISSN: 0025-7125 CODEN: MCNAA
CY United States
DT Journal; General Review
FS 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English

L6 ANSWER 15 OF 41 MEDLINE
TI Determinants of appropriate use of **angiotensin-converting enzyme inhibitors** after acute myocardial infarction in persons > or = 65 years of age.
SO AMERICAN JOURNAL OF CARDIOLOGY, **(1997 Mar 1)** 79 (5) 581-6.
Journal code: 3DQ; 0207277. ISSN: 0002-9149.
AB We sought to determine how often angiotensin-converting enzyme (**ACE**) **inhibitors** are prescribed as a discharge medication among eligible patients > or = 65 years old with an acute myocardial infarction; to identify patient characteristics associated with the decision to prescribe **ACE inhibitors**; and to determine the factors associated with the decision to obtain an evaluation of left ventricular function among patients who have no contraindications to **ACE inhibitors**. We addressed these aims with an observational study of consecutive elderly Medicare beneficiary survivors of an acute myocardial infarction hospitalized. . . in Alabama, Connecticut, Iowa, and Wisconsin between June 1992 and February 1993. Among the 5,453 patients without a contraindication to **ACE inhibitors** at discharge, 3,528 (65%) had an evaluation of left ventricular function. Of the 1,228 patients without a contraindication to **ACE inhibitors** who had a left ventricular ejection fraction < or = 40%, 548 (45%) were prescribed the medication at discharge. In a multivariable analysis, an increased prescribed use of **ACE inhibitors** at discharge was correlated with several factors, including **diabetes** mellitus, **congestive heart failure**, ventricular tachycardia, and loop diuretics as a discharge medication. Patients admitted after the publication of the Survival and Ventricular Enlargement (SAVE) trial were significantly more likely to receive **ACE inhibitors**, although the absolute improvement in utilization was small in the 6 months after the trial results were published. In conclusion, improving the identification of appropriate patients for **ACE inhibitors** and increasing the prescription of **ACE inhibitors** for ideal patients may provide an excellent opportunity

to improve care.
CT Check Tags: Female; Human; Male
Aged
Aged, 80 and over
Alabama
Angiotensin-Converting Enzyme Inhibitors: AD, administration & dosage
Angiotensin-Converting Enzyme Inhibitors: CT, contraindications
***Angiotensin-Converting Enzyme Inhibitors: TU, therapeutic use**
Connecticut
Controlled Clinical Trials
Decision Making
Diabetes Mellitus: CO, complications
Diuretics: AD, administration & dosage
Diuretics: TU, therapeutic use
Drug Utilization
Follow-Up Studies
Heart Failure, Congestive: CO, complications
Hospitalization
Iowa
Medicaid
Multivariate Analysis
*Myocardial Infarction: DT, drug therapy
Patient Discharge
Prescriptions, Drug
Retrospective Studies
Stroke Volume
Tachycardia, Ventricular: CO, complications
United States
Ventricular Function, Left
Wisconsin
CN 0 (**Angiotensin-Converting Enzyme Inhibitors**); 0 (Diuretics)
AN 97221466 MEDLINE
DN 97221466 PubMed ID: 9068512
TI Determinants of appropriate use of **angiotensin-converting enzyme inhibitors** after acute myocardial infarction in persons > or = 65 years of age.
AU Krumholz H M; Vaccarino V; Ellerbeck E F; Kiefe C; Hennen J; Kresowik T F;
Gold J A; Jencks S F; Radford M J
CS Department of Medicine, Yale School of Medicine, New Haven, Connecticut 06520-8017, USA.
SO AMERICAN JOURNAL OF CARDIOLOGY, **(1997 Mar 1)** 79 (5) 581-6.
Journal code: 3DQ; 0207277. ISSN: 0002-9149.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199704
ED Entered STN: 19970422
Last Updated on STN: 19970422
Entered Medline: 19970408

L6 ANSWER 16 OF 41 USPATFULL
PI US 5571893 19961105 <--
SUMM Current therapy for heart failure is primarily directed to using angiotensin-converting enzyme (**ACE**) **inhibitors** and diuretics. While prolonging survival in the setting of heart failure, **ACE inhibitors** appear to slow the progression towards end-stage heart failure, and substantial numbers of patients on **ACE inhibitors** have functional class III heart failure. Moreover, **ACE inhibitors** consistently appear unable to relieve symptoms in more than 60% of heart failure patients and reduce mortality of heart failure. . .
SUMM . . . activation of physiological or compensatory hypertrophy can be

beneficial in the setting of heart failure. In fact, the effects of **ACE inhibitors** have been purported not only to unload the heart, but also to inhibit the pathological hypertrophic response that has been. . .

SUMM Not only is there a need for an improvement in the therapy of heart failure such as **congestive heart failure,** but there is also a need to offer effective treatment for neurological disorders. Neurotrophic factors such as insulin-like growth factors,. .

. means for enhancing neuronal survival, for example, as a treatment for neurodegenerative diseases such as amyotrophic lateral sclerosis, Alzheimer's disease, **stroke**, epilepsy, Huntington's disease, Parkinson's disease, and peripheral neuropathy. It would be desirable to

provide an additional therapy for this purpose.

SUMM . . . object of the present invention to provide an improved therapy for the prevention and/or treatment of heart failure such as **congestive heart failure**, particularly the promotion of physiological forms of hypertrophy or inhibition of pathological forms of hypertrophy, and for the prevention and/or. . .

DETD . . . disorders include all neurodegenerative diseases, such as peripheral neuropathies (motor and sensory), amyotrophic lateral sclerosis (ALS), Alzheimer's disease, Parkinson's disease, **stroke**, Huntington's disease, epilepsy, and ophthalmologic diseases such as those involving the retina, e.g., diabetic retinopathy, retinal dystrophy, and retinal degeneration. . .

DETD . . . the rate needed for the requirements of metabolizing tissues. Heart failure includes a wide range of disease states such as **congestive heart failure**, myocardial infarction, and tachyarrhythmia.

DETD As used herein, **"ACE inhibitor"** refers to angiotensin-converting enzyme inhibiting drugs which prevent the conversion of angiotensin I to angiotensin II. The **ACE inhibitors** may be beneficial in **congestive heart failure** by reducing systemic vascular resistance and relieving circulatory congestion. The **ACE inhibitors** include but are not limited to those designated by the trademarks Accupril.RTM. (quinapril), Altace.RTM. (ramipril), Capoten.RTM. (captopril), Lorensin.RTM. (benazepril), Monopril.RTM. (fosinopril), Prinivil.RTM. (lisinopril), Vasotec.RTM. (enalapril), and Zestril.RTM. (lisinopril). One example of an **ACE inhibitor** is that sold under the trademark Capoten.RTM.. Generically referred to as captopril, this **ACE inhibitor** is designated chemically as 1-[(2S)-3-mercapto-2-methylpropionyl]-L-proline.

DETD . . . administering a therapeutically effective amount of a CHF to the mammal. Optionally, the CHF is administered in combination with an **ACE inhibitor**, such as captopril, in the case of **congestive heart failure**, or with another myocardiotrophic, anti-arrhythmic, or inotropic factor in the case of other types of heart failure or cardiac disorder,. . .

DETD For example, CHF may be useful in treating **congestive heart failure** in cases where **ACE inhibitors** cannot be employed or are not as effective. CHF optionally is combined with or administered in concert with other agents for treating **congestive heart failure,** including **ACE inhibitors.**

DETD The effective amount of **ACE inhibitor** to be administered, if employed, will be at the physician's or veterinarian's discretion. Dosage administration and adjustment is done to achieve optimal management of **congestive heart failure** and ideally takes into account use of diuretics or digitalis, and conditions such as hypotension and renal impairment. The dose. . . and the specific patient being treated. Typically the

amount employed will be the same dose as that used if the **ACE inhibitor** were to be administered without CHF.

DETD . . . administration in tablet or capsule form. A discussion of the dosage, administration, indications and contraindications associated with captopril and other **ACE inhibitors** can be found in the Physicians Desk Reference, Medical Economics Data Production Co., Montvale, N.J. 2314-2320 (1994).

DETD . . . into the treatment of all neurodegenerative diseases by CHF, including peripheral neuropathies (motor and sensory), ALS, Alzheimer's disease, Parkinson's disease, **stroke**, Huntington's disease, and ophthalmologic diseases, for example, those involving the retina.

DETD . . . be one which increases ventricular contractility and decreases peripheral vascular resistance or ameliorates or treats conditions of similar importance in **congestive heart failure** patients. The progress of this therapy is easily monitored by conventional assays.

DETD . . . endothelin, neonatal rat myocardial cells in culture display several features of the in vivo cardiac muscle cell hypertrophy seen in **congestive heart failure**, including an increase in cell size and an increase in the assembly of an individual contractile protein into organized contractile. . .

DETD . . . heart beat, concentric or dilated hypertrophy, left ventricular systolic pressure, left ventricular mean pressure, left ventricular end-diastolic pressure, cardiac output, **stroke** index, histological parameters, ventricular size, wall thickness, etc.

DETD The purified CHF is also tested in a post-myocardial infarction rat model, which is predictive of human **congestive heart failure** in producing natriuretic peptide. Specifically, male Sprague-Dawley rats (Charles River Breeding Laboratories, Inc., eight weeks of age) are acclimated to. . .

DETD In clinical patients, myocardial infarction or coronary artery disease is the most common cause of heart failure. **Congestive heart failure** in this model reasonably mimics **congestive heart failure** in most human patients.

DETD . . . curve is monitored by VR-16 simultrace recorders (Honeywell Co., N.Y.) and cardiac output (CO) is digitally obtained by the microcomputer. **Stroke** volume (SV)=CO/HR; Cardiac index (CI)=CO/BW; Systemic vascular resistance (SVR)=MAP/CI.

DETD . . . and ligated rat controls. This expected result would demonstrate that administration of CHF or CHF antagonist improves cardiac function in **congestive heart failure**. In sham rats, however, CHF or CHF antagonist administration at this dose is not expected to alter significantly cardiac function. . .

DETD . . . are determined at the time of re-evaluation, the dose would be adjusted upward. Concurrent medication doses (e.g., captopril as an **ACE inhibitor** and diuretics) would be adjusted at the discretion of the study physician. After the maximum dose is administered for 8. . .

DETD . . . or peak exercise VO.sub.2 <16 mL/kg/min. (adjusted for age), stable for at least one month on digoxin, diuretics, and vasodilators (**ACE inhibitors**).

DETD Concurrent **ACE inhibitor** therapy.

DETD **Diabetes** mellitus or impaired glucose tolerance.

AN 96:101657 USPATFULL

TI Cardiac hypertrophy factor

IN Baker, Joffre, El Granada, CA, United States
Chien, Kenneth, La Jolla, CA, United States
King, Kathleen, Pacifica, CA, United States
Pennica, Diane, Burlingame, CA, United States
Wood, William, San Mateo, CA, United States

PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
Regents of the Univ. of California, Oakland, CA, United States (U.S.

corporation)
PI US 5571893 19961105 <--
AI US 1994-286304 19940805 (8)
RLI Continuation of Ser. No. US 1994-233609, filed on 25 Apr 1994, now patented, Pat. No. US 5534615
DT Utility
EXNAM Primary Examiner: Draper, Garnette D.; Assistant Examiner: Hayes, Robert C.
LREP Torchia, Timothy E.; Hasak, Janet E.
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN 8 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 4056
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 17 OF 41 USPATFULL
PI US 5571675 19961105 <--
SUMM Current therapy for heart failure is primarily directed to using angiotensin-converting enzyme (**ACE**) **inhibitors** and diuretics. While prolonging survival in the setting of heart failure, **ACE inhibitors** appear to slow the progression towards end-stage heart failure, and substantial numbers of patients on **ACE inhibitors** have functional class III heart failure. Moreover, **ACE inhibitors** consistently appear unable to relieve symptoms in more than 60% of heart failure patients and reduce mortality of heart failure. . .
SUMM . . . activation of physiological or compensatory hypertrophy can be beneficial in the setting of heart failure. In fact, the effects of **ACE inhibitors** have been purported not only to unload the heart, but also to inhibit the pathological hypertrophic response that has been. . .
SUMM Not only is there a need for an improvement in the therapy of heart failure such as **congestive heart failure**, but there is also a need to offer effective treatment for neurological disorders. Neurotrophic factors such as insulin-like growth factors,.
.
. means for enhancing neuronal survival, for example, as a treatment for neurodegenerative diseases such as amyotrophic lateral sclerosis, Alzheimer's disease, **stroke**, epilepsy, Huntington's disease, Parkinson's disease, and peripheral neuropathy. It would be desirable to provide an additional therapy for this purpose.
SUMM . . . object of the present invention to provide an improved therapy for the prevention and/or treatment of heart failure such as **congestive heart failure**, particularly the promotion of physiological forms of hypertrophy or inhibition of pathological forms of hypertrophy, and for the prevention and/or. . .
DETD . . . disorders include all neurodegenerative diseases, such as peripheral neuropathies (motor and sensory), amyotrophic lateral sclerosis (ALS), Alzheimer's disease, Parkinson's disease, **stroke**, Huntington's disease, epilepsy, and ophthalmologic diseases such as those involving the retina, e.g., diabetic retinopathy, retinal dystrophy, and retinal degeneration. . .
DETD . . . the rate needed for the requirements of metabolizing tissues. Heart failure includes a wide range of disease states such as **congestive heart failure**, myocardial infarction, and tachyarrhythmia.
DETD As used herein, **"ACE inhibitor"** refers to angiotensin-converting enzyme inhibiting drugs which prevent the conversion of angiotensin I to angiotensin II. The **ACE inhibitors** may be beneficial in **congestive heart failure** by reducing systemic vascular resistance and relieving circulatory congestion. The **ACE inhibitors** include but are not limited to those designated by

the trademarks Accupril.RTM. (quinapril), Altace.RTM. (ramipril), Capoten.RTM. (captopril), Lotensin.RTM. (benazepril), Monopril.RTM. (fosinopril), Prinivil.RTM. (lisinopril), Vasotec.RTM. (enalapril), and Zestril.RTM. (lisinopril). One example of an **ACE inhibitor** is that sold under the trademark Capoten.RTM.. Generically referred to as captopril, this **ACE inhibitor** is designated chemically as 1-[(2S)-3-mercapto-2-methylpropionyl]-L-proline.

DETD . . . administering a therapeutically effective amount of a CHF to the mammal. Optionally, the CHF is administered in combination with an **ACE inhibitor**, such as captopril, in the case of **congestive heart failure**, or with another myocardiotrophic, anti-arrhythmic, or inotropic factor in the case of other types of heart failure or cardiac disorder,. . .

DETD For example, CHF may be useful in treating **congestive heart failure** in cases where **ACE inhibitors** cannot be employed or are not as effective. CHF optionally is combined with or administered in concert with other agents for treating **congestive heart failure**, including **ACE inhibitors**.

DETD The effective amount of **ACE inhibitor** to be administered, if employed, will be at the physician's or veterinarian's discretion. Dosage administration and adjustment is done to achieve optimal management of **congestive heart failure** and ideally takes into account use of diuretics or digitalis, and conditions such as hypotension and renal impairment. The dose. . . and the specific patient being treated. Typically the amount employed will be the same dose as that used if the **ACE inhibitor** were to be administered without CHF.

DETD . . . administration in tablet or capsule form. A discussion of the dosage, administration, indications and contraindications associated with captopril and other **ACE inhibitors** can be found in the Physicians Desk Reference, Medical Economics Data Production Co., Montvale, N.J. 2314-2320 (1994).

DETD . . . into the treatment of all neurodegenerative diseases by CHF, including peripheral neuropathies (motor and sensory), ALS, Alzheimer's disease, Parkinson's disease, **stroke**, Huntington's disease, and ophthalmologic diseases, for example, those involving the retina.

DETD . . . be one which increases ventricular contractility and decreases peripheral vascular resistance or ameliorates or treats conditions of similar importance in **congestive heart failure** patients. The progress of this therapy is easily monitored by conventional assays.

DETD . . . endothelin, neonatal rat myocardial cells in culture display several features of the in vivo cardiac muscle cell hypertrophy seen in **congestive heart failure**, including an increase in cell size and an increase in the assembly of an individual contractile protein into organized contractile. . .

DETD . . . heart beat, concentric or dilated hypertrophy, left ventricular systolic pressure, left ventricular mean pressure, left ventricular end-diastolic pressure, cardiac output, **stroke** index, histological parameters, ventricular size, wall thickness, etc.

DETD The purified CHF is also tested in a post-myocardial infarction rat model, which is predictive of human **congestive heart failure** in producing natriuretic peptide. Specifically, male Sprague-Dawley rats (Charles River Breeding Laboratories, Inc., eight weeks of age) are acclimated to. . .

DETD In clinical patients, myocardial infarction or coronary artery disease is the most common cause of heart failure. **Congestive heart failure** in this model reasonably mimics **congestive heart failure** in most human patients.

DETD . . . is monitored by VR-16 simultrace recorders (Honeywell Co., New

York) and cardiac output (CO) is digitally obtained by the microcomputer. **Stroke** volume (SV)=CO/HR; Cardiac index (CI)=CO/BW; Systemic vascular resistance (SVR)=MAP/CI.

DETD . . . and ligated rat controls. This expected result would demonstrate that administration of CHF or CHF antagonist improves cardiac function in **congestive heart failure**. In sham rats, however, CHF or CHF antagonist administration at this dose is not expected to alter significantly cardiac function. . .

DETD . . . are determined at the time of re-evaluation, the dose would be adjusted upward. Concurrent medication doses (e.g., captopril as an **ACE inhibitor** and diuretics) would be adjusted at the discretion of the study physician. After the maximum dose is administered for 8. . .

DETD . . . or peak exercise VO.sub.2 <16 mL/kg/min. (adjusted for age), stable for at least one month on digoxin, diuretics, and vasodilators (**ACE inhibitors**).

DETD Concurrent **ACE inhibitor** therapy.

DETD **Diabetes** mellitus or impaired glucose tolerance.

AN 96:101443 USPATFULL

TI Detection and amplification of candiotrophin-1(cardiac hypertrophy factor)

IN Baker, Joffre, El Granada, CA, United States
Chien, Kenneth, La Jolla, CA, United States
King, Kathleen, Pacifica, CA, United States
Pennica, Diane, Burlingame, CA, United States
Wood, William, San Mateo, CA, United States

PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
Regents of the Univ. of California, Oakland, CA, United States (U.S. corporation)

PI US 5571675 19961105 <--

AI US 1995-444083 19950517 (8)

RLI Division of Ser. No. US 1994-286304, filed on 5 Aug 1994 which is a continuation-in-part of Ser. No. US 1994-233609, filed on 25 Apr 1994

DT Utility

EXNAM Primary Examiner: Zitomer, Stephanie W.; Assistant Examiner: Fredman, Jeffrey

LREP Torchia, Timothy E.; Hasak, Janet E.

CLMN Number of Claims: 14

ECL Exemplary Claim: 1

DRWN 6 Drawing Figure(s); 8 Drawing Page(s)

LN.CNT 4298

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 18 OF 41 USPATFULL

PI US 5554625 19960910 <--
WO 9402142 19940203 <--

SUMM . . . the regulation of normal blood pressure and seems to be critically involved in hypertension development and maintenance as well as **congestive heart failure**. Angiotensin II (A II) is an octapeptide hormone produced mainly in the blood during the cleavage of angiotensin I by. . .

SUMM . . . of the right eye and down the spinal column. The rats were immediately placed on a Harvard Rodent Ventilator (rate--60 **strokes** per minute, volume--1.1 cc per 100 grams body weight). The right carotid artery was ligated, both left and right vagal. . .

SUMM . . . of the invention are useful in treating hypertension. They are also of value in the management of acute and chronic **congestive heart failure** and angina. These compounds are also expected to be useful in primary and secondary hyperaldosteronism, renal diseases such as diabetic. . . minimize the atherosclerotic process, in neointimal hyperplasia follwoing angioplasty or vascular injury and to retard the onset of type II **diabetes**. The application of the compounds of this invention for these and similar disorders will be

apparent to those skilled in. . .
SUMM . . . diltiazem, felodipine, nifedipine, amlodipine, nimodipine, isradipinei nitrendipine and verapamil; .beta.-adrenergic antagonists such as timolol, atenolol, metoprolol, propanolol; nadolol and pindolol;
angiotensin converting enzyme inhibitors such as enalapril, lisinopril, captopril, ramipril, quinapril and zofenopril; renin inhibitors such as A-69729 and FK 906 and FK 744;. . .
SUMM Combinations useful in the management of **congestive heart failure** include, in addition, compounds of this invention with cardiac stimulants such as dobutamine and xamoterol and phosphodiesterase inhibitors including amrinone. . .
DETD . . . can also include a pharmaceutically effective amount of another active ingredient such as another antihypertansive and/or a diuretic and/or an **angiotensin converting enzyme inhibitor** and/or a calcium channel blocker.
AN 96:82697 USPATFULL
TI Substituted biphenylmethylimidazopyridines
IN Rivero, Ralph A., Tinton Falls, NJ, United States
Chakravarty, Prasun K., Edison, NJ, United States
Greenlee, William J., Teaneck, NJ, United States
Kevin, Nancy J., Clifton, NJ, United States
Mantlo, Nathan B., Westfield, NJ, United States
PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)
PI US 5554625 19960910 <--
WO 9402142 19940203 <--
AI US 1995-416790 19950106 (8)
WO 1993-US6407 19930707
19950106 PCT 371 date
19950106 PCT 102(e) date
RLI Continuation of Ser. No. US 1992-916303, filed on 17 Jul 1992, now abandoned
DT Utility
EXNAM Primary Examiner: Dentz, Bernard
LREP Camara, Valerie J.; Daniel, Mark R.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1292
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 19-48 kwic bib

L6 ANSWER 19 OF 41 USPATFULL
PI US 5545651 19960813 <--
SUMM . . . these novel imidazoles and pharmaceutical methods using them, alone and in conjugation with other drugs, especially diuretics, angiotensin converting enzyme (**ACE**) **inhibitors**, and non-steroidal anti-inflammatory drugs (NSAIDS).
SUMM . . . (II) or (III), and methods of using the novel compounds of Formula (I), (II) or (III), to treat hypertension and **congestive heart failure**. The pharmaceutical compositions can optionally contain one or more other therapeutic agents, such as a diuretic, an angiotensin I converting enzyme (**ACE**) **inhibitor** or a non-steroidal antiinflammatory drug (NSAID). Also within the scope of this invention is a method of preventing renal failure. . .
DETD . . . treating hypertension, and for the treatment of hyperuricemia, primary and secondary hyperaldosteronism, psoriasis, cardiac disorders such as acute and chronic **congestive heart failure**, angina pectoris, myocardial infarction, systolic and diastolic dysfunction, cardiac myopathy, and cardiac hypertrophy and

hyperplasia, esp. left ventricular hypertrophy; pulmonary. . . or bypass surgery, vascular hypertrophy and hyperplasia, atheroma and Raynaud's disease; cerebrovascular disorders such as migraine, and ischemic and hemorragic **stroke**; renal disorders such as renal vascular hypertension, proteinuria of primary renal disease, end stage renal disease and renal transplant therapy,. . . and tardive dyskinesia; ocular disorders such as macular degeneration and elevated intraocular pressure; gastrointestinal and bladder disorders; disorders associated with **diabetes**, such as diabetic angiopathy, nephropathy and retinopathy, and for delaying the onset of type II **diabetes**. The application of the compounds of this invention for these and similar disorders will be apparent to those skilled in. . .

DETD . . . diltiazem, felodipine, nifedipine, amLodipine, nimodipine, isradipine, nitrendipine and verapamil; b-adrenergic antagonists such as timolol, atenolol, metoprolol, propanolol, nadolol and pindolol; **angiotensin converting enzyme inhibitors** such as enalapril, lisinopril, captopril, ramipril, quinapril and zofenopril; renin inhibitors such as A-69729, FK 906 and FK 744; a-adrenergic. . . guanethidine, hydralazine hydrochloride and sodium nitroprusside as well as combinations of the above-named drugs. Combinations useful in the management of **congestive heart failure** include, in addition, compounds of this invention with cardiac stimulants such as dobutamine and xamoterol and phosphodiesterase inhibitors including atarinone. . .

CLM What is claimed:

5. A method of treating **congestive heart failure** in a warm-blooded animal comprising administering to said animal in need of such treatment and effective amount of a compound. . .

AN 96:72899 USPATFULL|

TI Imidazole 5-position substituted angiotensin II antagonists|

IN Duncia, John J. V., Wilmington, DE, United States
Ensinger, Carol L., Newark, DE, United States
Olson, Richard E., Wilmington, DE, United States
Quan, Mimi L., Newark, DE, United States
Santella, III, Joseph B., Springfield, PA, United States
Vanatten, Mary K., Wilmington, DE, United States

PA The DuPont Merck Pharmaceutical Company, Wilmington, DE, United States (U.S. corporation)

PI US 5545651 19960813 <--

AI US 1994-348843 19941128 (8)

RLI Division of Ser. No. US 1993-72977, filed on 10 Jun 1993, now patented, Pat. No. US 5395844

DT Utility|

EXNAM Primary Examiner: Davis, Zinna Northington|

CLMN Number of Claims: 5|

ECL Exemplary Claim: 1|

DRWN No Drawings

LN.CNT 5010|

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 20 OF 41 USPATFULL

PI US 5534615 19960709 <--

SUMM Current therapy for heart failure is primarily directed to using angiotensin-converting enzyme (**ACE**) **inhibitors** and diuretics. While prolonging survival in the setting of heart failure, **ACE inhibitors** appear to slow the progression towards end-stage heart failure, and substantial numbers of patients on **ACE inhibitors** have functional class III heart failure. Moreover, **ACE inhibitors** consistently appear unable to relieve symptoms in more than 60% of heart failure patients and reduce mortality of heart failure. . .

SUMM . . . activation of physiological or compensatory hypertrophy can be beneficial in the setting of heart failure. In fact, the effects of

ACE inhibitors have been purported not only to unload the heart, but also to inhibit the pathological hypertrophic response that has been. . .

SUMM Not only is there a need for an improvement in the therapy of heart failure such as **congestive heart failure**, but there is also a need to offer effective treatment for neurological disorders. Neurotrophic factors such as insulin-like growth factors,. .

. means for enhancing neuronal survival, for example, as a treatment for neurodegenerative diseases such as amyotrophic lateral sclerosis, Alzheimer's disease, **stroke**, epilepsy, Huntington's disease, Parkinson's disease, and peripheral neuropathy. It would be desirable to provide an additional therapy for this purpose.

SUMM . . . object of the present invention to provide an improved therapy for the prevention and/or treatment of heart failure such as **congestive heart failure**, particularly the promotion of physiological forms of hypertrophy or inhibition of pathological forms of hypertrophy, and for the prevention and/or. . .

DETD . . . disorders include all neurodegenerative diseases, such as peripheral neuropathies (motor and sensory), amyotrophic lateral sclerosis (ALS), Alzheimer's disease, Parkinson's disease, **stroke**, Huntington's disease, epilepsy, and ophthalmologic diseases such as those involving the retina, e.g., diabetic retinopathy, retinal dystrophy, and retinal degeneration. . .

DETD . . . the rate needed for the requirements of metabolizing tissues. Heart failure includes a wide range of disease states such as **congestive heart failure**, myocardial infarction, and tachyarrhythmia.

DETD . . . administering a therapeutically effective amount of a CHF to the mammal. Optionally, the CHF is administered in combination with an **ACE inhibitor**, such as Captopril.TM. **ACE inhibitor**, in the case of **congestive heart failure**, or with another myocardiotrophic, anti-arrhythmic, or inotropic factor in the case of other types of heart failure or cardiac disorder,. . .

DETD . . . disorders involving motor neurons or other neurons in which CNTF is active. For example, CHF may be useful in treating **congestive heart failure** in cases where **ACE inhibitors** cannot be employed or are not as effective. CHF optionally is combined with or administered in concert with other agents for treating **congestive heart failure**, including **ACE inhibitors**.

DETD . . . into the treatment of all neurodegenerative diseases by CHF, including peripheral neuropathies (motor and sensory), ALS, Alzheimer's disease, Parkinson's disease, **stroke**, Huntington's disease, and ophthalmologic diseases, for example, those involving the retina.

DETD . . . be one which increases ventricular contractility and decreases peripheral vascular resistance or ameliorates or treats conditions of similar importance in **congestive heart failure** patients. The progress of this therapy is easily monitored by conventional assays.

DETD . . . endothelin, neonatal rat myocardial cells in culture display several features of the in vivo cardiac muscle cell hypertrophy seen in **congestive heart failure**, including an increase in cell size and an increase in the assembly of an individual contractile protein into organized contractile. . .

DETD . . . heart beat, concentric or dilated hypertrophy, left ventricular systolic pressure, left ventricular mean pressure, left ventricular end-diastolic pressure, cardiac output, **stroke** index, histological parameters, ventricular size, wall thickness, etc.

DETD The purified CHF is also tested in a post-myocardial infarction rat model, which is predictive of human **congestive heart failure** in producing natriuretic peptide. Specifically, male

Sprague-Dawley rats (Charles River Breeding Laboratories, Inc., eight weeks of age) are acclimated to. . .

DETD In clinical patients, myocardial infarction or coronary artery disease is the most common cause of heart failure. **Congestive heart failure** in this model reasonably mimics **congestive heart failure** in most human patients.

DETD . . . curve is monitored by VR-16 simultrace recorders (Honeywell Co., N.Y.) and cardiac output (CO) is digitally obtained by the microcomputer. **Stroke** volume (SV)=CO/HR; Cardiac index (CI)=CO/BW; Systemic vascular resistance (SVR)=MAP/CI.

DETD . . . and ligated rat controls. This expected result would demonstrate that administration of CHF or CHF antagonist improves cardiac function in **congestive heart failure** . In sham rats, however, CHF or CHF antagonist administration at this dose is not expected to alter significantly cardiac function. . .

DETD . . . effects are determined at the time of re-evaluation, the dose would be adjusted upward. Concurrent medication doses (e.g., Captopril.TM. brand **ACE inhibitor** and diuretics) would be adjusted at the discretion of the study physician. After the maximum dose is administered for 8. . .

DETD . . . or peak exercise VO.sub.2 <16 mL/kg/min. (adjusted for age), stable for at least one month on digoxin, diuretics, and vasodilators (**ACE inhibitors**).

DETD Concurrent **ACE inhibitor** therapy.

DETD **Diabetes** mellitus or impaired glucose tolerance.

AN 96:60798 USPATFULL

TI Cardiac hypertrophy factor and uses therefor

IN Baker, Joffre, El Granada, CA, United States
Chien, Kenneth, La Jolla, CA, United States
King, Kathleen, Pacifica, CA, United States
Pennice, Diane, Burlingame, CA, United States
Wood, William, San Mateo, CA, United States

PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
The Regents of the University of California, Oakland, CA, United States (U.S. corporation)

PI US 5534615 19960709 <--

AI US 1994-233609 19940425 (8)

DT Utility

EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Kim, Hyosuk

LREP Hasak, Janet E.; Torchia, Timothy E.

CLMN Number of Claims: 1

ECL Exemplary Claim: 1

DRWN 5 Drawing Figure(s); 5 Drawing Page(s)

LN.CNT 3897

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 21 OF 41 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

SO American Family Physician, (1996) 53/8 (2553-2560).
ISSN: 0002-838X CODEN: AFPYAE

AB Although calcium channel blockers and angiotensin-converting enzyme (**ACE**) **inhibitors** are effective in lowering blood pressure, no long-term data show their effect on morbidity and mortality in hypertensive patients. They. . . at all in the treatment of hypertension. Nonhydropyridine calcium channel blockers may reduce the incidence of second infarction but not **congestive heart failure** or mortality in patients with ischemic heart disease. The **ACE inhibitors** increase insulin sensitivity and decrease intraglomerular pressure. In combination with a diuretic, they are the preferred agents in the treatment of diabetic patients with hypertension, especially those with nephropathy. In both hypertensive and normotensive patients, **ACE inhibitors** reduce morbidity and mortality resulting from **congestive heart failure** in patients with poor left ventricular function who are also being treated with a diuretic and/or digitalis. They do not, however,

reduce **strokes** or myocardial infarctions in hypertensive patients.

CT Medical Descriptors:
*hypertension: DT, drug therapy
adjuvant disease
angioneurotic edema: SI, side effect
antihypertensive activity
article
congestive heart failure
coughing: SI, side effect
diabetes mellitus
drug effect
drug efficacy
gastrointestinal symptom: SI, side effect
heart palpitation: SI, side effect
human
kidney disease
treatment planning
*enalapril: DT, drug therapy
*enalapril: AE, adverse drug. . .

AN 96185749 EMBASE
DN 1996185749
TI Management of hypertension, part II.
AU Moser M.
SO American Family Physician, (1996) 53/8 (2553-2560).
ISSN: 0002-838X CODEN: AFPYAE
CY United States
DT Journal; Article
FS 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English

L6 ANSWER 22 OF 41 USPATFULL
PI US 5411980 19950502 <--
SUMM . . . triazolinimine compounds and derivatives thereof which are useful as angiotensin II antagonists in the treatment of elevated blood pressure and **congestive heart failure**.
Thus, the substituted triazolinone, triazolinethione and triazolinimine compounds of the invention are useful as antihypertensives.
SUMM . .. . the regulation of normal blood pressure and seems to be critically involved in hypertension development and maintenance as well as **congestive heart failure**. Angiotensin
II (A II) is an octapeptide hormone produced mainly in the blood during the cleavage of angiotensin I by. . .
SUMM . . . novel substituted triazole compounds and derivatives thereof which are useful as angiotensin II antagonists, as antihypertensives, in
the treatment of **congestive heart failure**
and in the treatment of elevated intraocular pressure. The compounds of this invention have the general formula (I): ##STR3## wherein. . .
SUMM . . . of the right eye and down the spinal column. The rats were immediately placed on a Harvard Rodent Ventilator (rate--60 **strokes** per minute, volume--1.1 cc per 100 grams body weight).
The right carotid artery was ligated, both left and right vagal. . .

SUMM . . . of the invention are useful in treating hypertension. They are also of value in the management of acute and chronic **congestive heart failure** and angina. These compounds are also
expected to be useful in primary and secondary hyperaldosteronism, renal
diseases such as diabetic. . . minimize the atherosclerotic process, in neointimal hyperplasia following angioplasty or vascular injury and to retard the onset of type II **diabetes**. The application of
the compounds of this invention for these and similar disorders will be

apparent to those skilled in. . .
SUMM . . . diltiazem, felodipine, nifedipine, amlodipine, nimodipine, isradipine, nitrendipine and verapamil; .beta.-adrenergic antagonists such as timolol, atenolol, metoprolol, propanolol, nadolol and pindolol;
angiotensin converting enzyme
inhibitors such as enalapril, lisinopril, captopril, ramipril, quinapril and zofenopril; renin inhibitors such as A-69729 and FK 906 and FK 744;. . .
SUMM Combinations useful in the management of **congestive heart failure** include, in addition, compounds of this invention with cardiac stimulants such as dobutamine and xamoterol and phosphodiesterase inhibitors including amrinone. . .
DETD . . . can also include a pharmaceutically effective amount of another active ingredient such as another antihypertensive and/or a diuretic and/or an **angiotensin converting enzyme** **inhibitor** and/or a calcium channel blocker.
AN 95:38691 USPATFULL
TI Substituted triazolinones, triazolinethiones, and triazolinimines as angiotensin II antagonists
IN Ashton, Wallace T., Clark, NJ, United States
Chang, Linda L., Wayne, NJ, United States
MacCoss, Malcolm, Freehold, NJ, United States
Chakravarty, Prasun K., Edison, NJ, United States
Greenlee, William J., Teaneck, NJ, United States
Patchett, Arthur A., Westfield, NJ, United States
Flanagan, Kelly, Edison, NJ, United States
PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)
PI US 5411980 19950502 <--
AI US 1992-994228 19921221 (7)
RLI Continuation-in-part of Ser. No. US 1992-899868, filed on 17 Dec 1992, now abandoned And Ser. No. US 1991-812891, filed on 20 Dec 1991, now abandoned which is a continuation-in-part of Ser. No. US 1991-725720, filed on 3 Jul 1991, now abandoned which is a continuation-in-part of Ser. No. US 1990-504507, filed on 4 Apr 1990, now abandoned which is a continuation-in-part of Ser. No. US 1989-386328, filed on 28 Jul 1989, now abandoned
DT Utility
EXNAM Primary Examiner: Morris, Patricia L.
LREP Camara, Valerie J.; Daniel, Mark R.; DiPrima, Joseph F.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 7039
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 23 OF 41 USPATFULL
PI US 5395844 19950307 <--
SUMM . . . these novel imidazoles and pharmaceutical methods using them, alone and in conjugation with other drugs, especially diuretics, angiotensin converting enzyme (**ACE**) **inhibitors**, and non-steroidal anti-inflammatory drugs (NSAIDS).
SUMM . . . (II) or (III), and methods of using the novel compounds of Formula (I), (II) or (III), to treat hypertension and **congestive heart failure**. The pharmaceutical compositions can optionally contain one or more other therapeutic agents, such as a diuretic, an angiotensin I converting enzyme (**ACE**) **inhibitor** or a non-steroidal antiinflammatory drug (NSAID). Also within the scope of this invention is a method of preventing renal failure. . .
DETD . . . treating hypertension, and for the treatment of hyperuricemia, primary and secondary hyperaldosteronism, psoriasis, cardiac disorders such as acute and chronic **congestive heart failure**, angina pectoris, myocardial infarction, systolic and diastolic dysfunction, cardiac myopathy, and cardiac hypertrophy and

hyperplasia, esp. left ventricular hypertrophy; pulmonary. . . or bypass surgery, vascular hypertrophy and hyperplasia, atheroma and Raynaud's disease; cerebrovascular disorders such as migraine, and ischemic and hemorragic **stroke**; renal disorders such as renal vascular hypertension, proteinuria of primary renal disease, end stage renal disease and renal transplant therapy,. . . and tardive dyskinesia; ocular disorders such as macular degeneration and elevated intraocular pressure; gastrointestinal and bladder disorders; disorders associated with **diabetes**, such as a diabetic angiopathy, nephropathy and retinopathy, and for delaying the onset of type II **diabetes**. The application of the compounds of this invention for these and similar disorders will be apparent to those skilled in. . .

DETD . . . guanethidine, hydralazine hydrochloride and sodium nitroprusside as well as combinations of the above-named drugs. Combinations useful in the management of **congestive heart failure** include, in addition, compounds of this invention with cardiac stimulants such as dobutamine and xamoterol and phosphodiesterase inhibitors including amrinone. . .

CLM What is claimed:
5. A method of treating **congestive heart failure** in a warn blooded animal comprising administering to said animal in need of such treatment an effective amount of a. . .

AN 95:20736 USPATFULL|
TI Imidazole 5-position substituted angiotensin II antagonists|
IN Duncia, John J. V., Wilmington, DE, United States
Ensinger, Carol L., Newark, DE, United States
Olson, Richard E., Wilmington, DE, United States
Quan, Mimi L., Newark, DE, United States
Santella, III, Joseph B., Springfield, PA, United States
Vanatten, Mary K., Wilmington, DE, United States
PA The Du Pont Merck Pharmaceutical Company, Wilmington, DE, United States (U.S. corporation)
PI US 5395844 19950307 <--
AI US 1993-72977 19930610 (8)
DT Utility|
EXNAM Primary Examiner: Ivy, C. Warren; Assistant Examiner: Davis, Zinna N.|
CLMN Number of Claims: 5|
ECL Exemplary Claim: 1|
DRWN No Drawings
LN.CNT 5135|
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 24 OF 41 USPATFULL
PI US 5376666 19941227 <--

SUMM . . . containing these imidazoles and pharmaceutical methods using them, alone and in conjugation with other drugs, especially diuretics, angiotensin converting enzyme (**ACE**) **inhibitors**, and non-steroidal anti-inflammatory drugs (NSAIDS).

SUMM . . . Number 90305850.1 (EP 400,974) discloses imidazo-fused 6-membered heterocycles (C) as angiotensin II antagonists useful in the treatment of hypertension and **congestive heart failure**, where A, B, C, ##STR3## and C are independently carbon or nitrogen atoms.

SUMM . . . a novel compound of Formula (I), and methods of using the novel compounds of Formula (I) to treat hypertension and **congestive heart failure**. The pharmaceutical compositions can optionally contain one or more other therapeutic agents, such as a diuretic, an angiotensin I converting enzyme (**ACE**) **inhibitor** or a non-steroidal antiinflammatory drug (NSAID). Also within the scope of this invention is a method of preventing renal failure. . .

DETD . . . treating hypertension, and for the treatment of hyperuricemia, primary and secondary hyperaldosteronism, psoriasis, cardiac disorders such as acute and chronic **congestive heart failure**, angina pectoris, myocardial infarction, systolic and

diastolic dysfunction, cardiac myopathy, and cardiac hypertrophy and hyperplasia, esp. left ventricular hypertrophy; pulmonary. . . . or bypass surgery, vascular hypertrophy and hyperplasia, atheroma and Raynaud's disease; cerebrovascular disorders such as migraine, and ischemic and hemorragic **stroke**; renal disorders such as renal vascular hypertension, proteinuria of primary renal disease, end stage renal disease and renal transplant therapy,. . . and tardive dyskinesia; ocular disorders such as macular degeneration and elevated intraocular pressure; gastrointestinal and bladder disorders; disorders associated with **diabetes**, such as diabetic angiopathy, nephropathy and retinopathy, and for delaying the onset of type II **diabetes**. The application of the compounds of this invention for these and similar disorders will be apparent to those skilled in. . .

DETD . . . diltiazem, felodipine, nifedipine, amlodipine, nimodipine, isradipine, nitrendipine and verapamil; b-adrenergic antagonists such as timolol, atenolol, metoprolol, propanolol, nadolol and pindolol; **angiotensin converting enzyme inhibitors** such as enalapril, lisinopril, captopril, ramipril, quinapril and zofenopril; renin inhibitors such as A-69729, FK 906 and FK 744; a-adrenergic. . . guanethidine, hydralazine hydrochloride and sodium nitroprusside as well as combinations of the above-named drugs. Combinations useful in the management of **congestive heart failure** include, in addition, compounds of this invention with cardiac stimulants such as dobutamine and xamoterol and phosphodiesterase inhibitors including amrinone. . .

CLM What is claimed is:

7. A method of treating **congestive heart failure** in a warm blooded animal comprising administering to an animal in need of such treatment an effective amount of a. . .

AN 94:113029 USPATFULL|

TI Angiotension-II receptor blocking, azacycloalkyl or azacycloalkenyl|

IN Duncia, John J. V., Wilmington, DE, United States

PA The Du Pont Merck Pharmaceutical Company, Wilmington, DE, United States (U.S. corporation)

PI US 5376666 19941227 <--

AI US 1992-983307 19921130 (7)

DT Utility|

EXNAM Primary Examiner: Dentz, Bernard|

LREP Reinert, Norbert F.|

CLMN Number of Claims: 7|

ECL Exemplary Claim: 1|

DRWN No Drawings

LN.CNT 1597|

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 25 OF 41 USPATFULL

PI US 5308846 19940503 <--

AB . . . ##STR1## are angiotensin II antagonists useful in the treatment of disorders related to the renin-angiotensin system (RAS) such as hypertension, **congestive heart failure**, ocular hypertension and certain CNS disorders.

SUMM . . . compounds are angiotensin II antagonists useful in the treatment of disorders related to the renin-angiotensin system such as hypertension, and **congestive heart failure**.

SUMM . . . the regulation of normal blood pressure and seems to be critically involved in hypertension development and maintenance as well as **congestive heart failure**. Angiotension II (AII), an octapeptide hormone is produced mainly in the blood during the cleavage of angiotensin I by angiotension. . .

DETD . . . of the right eye and down the spinal column. The rats were immediately placed on a Harvard Roden Ventilator (rate--60 **strokes** per minute, volume--1.1 cc per 100 grams body weight).

The right carotid artery was ligated, both left and right vagal. . .

DETD . . . of the invention are useful in treating hypertension. They are also of value in the management of acute and chronic **congestive heart failure** and angina. These compounds may also be expected to be useful in the treatment of primary and secondary hyperaldosteronism; renal. . . minimize the atherosclerotic process and neointimal hyperplasia following angioplasty or vascular injury and to retard the onset of type II **diabetes**. The application of the compounds of this invention for these and similar disorders will be apparent to those skilled in. . .

DETD . . . diltiazem, felodipine, nifedipine, amlodipine, minodipine, isradipine, nitrendipine and verapamil; .beta.-adrenergic antagonists such as timolol, atenolol, metoprolol, propanolol, nadolol and pindolol; **angiotensin converting enzyme inhibitors** such as enalapril, lisinopril, captopril, ramipril, quinapril and zofenopril; renin inhibitors such as A-69729, FK 906 and FK 744; .alpha.-adrenergic. . .

DETD Combinations useful in the management of **congestive heart failure** include, in addition, compounds of this invention with cardiac stimulants such as dobutamine and xamoterol and phosphodiesterase inhibitors including amrinone. . .

AN 94:37943 USPATFULL

TI Quinazolinones

IN Allen, Eric E., Somerset, NJ, United States
Olson, Richard E., Wilmington, DE, United States

PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)
E. I. Du Pont de Nemours and Co., Wilmington, DE, United States (U.S. corporation)

PI US 5308846 19940503 <--

AI US 1993-96125 19930722 (8)

RLI Continuation of Ser. No. US 1992-923273, filed on 31 Jul 1992, now patented, Pat. No. US 5256667 which is a continuation-in-part of Ser. No. US 1991-765626, filed on 25 Sep 1991, now patented, Pat. No. US 5202322

DT Utility

EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Gupta, Y. N.

LREP Camara, Valerie J.; Daniel, Mark R.; DiPrima, Joseph F.

CLMN Number of Claims: 9

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1616

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 26 OF 41 USPATFULL

PI US 5284839 19940208 <--
WO 9200079 19920109 <--

SUMM . . . vascular system, the heart, blood vessels and the peripheral circulation such as vasospasm, angina, hemorrhage, high blood pressure, cardiac hypertrophy, **congestive heart failure** and myocardial infarction;

SUMM Cerebral diseases and diseases related to the central nervous system such as **stroke** and conditions associated with **stroke**, cerebral vasospasm and hemorrhage and depression;

SUMM **Diabetes** or complications of **diabetes**;

SUMM Cerebral diseases and diseases related to the central nervous system such as cerebral infarction, **stroke** and conditions related to **stroke**, cerebral vasospasm and hemorrhage, depression and dementia;

SUMM . . . other pharmaceutically active compound is for example selected from the group of .alpha.-adrenergic blocking agents, .beta.-adrenergic blocking agents, calcium-channel blockers, **ACE-inhibitors** and diuretics.

DETD . . . shows the counteractive effect of IP.sub.3 against NPY-induced food intake. In example 5 the combination therapy of IP.sub.3 and an

ACE-inhibitor is demonstrated in reducing high blood pressure.

DETD . . . a very potent inhibition of vessel constriction, which is a dominant component in diseases and conditions such as vasospasm, angina, **stroke** and hypertension.

DETD . . . vasoconstriction. These effects demonstrate a very potent effect of IP.sub.3 to reduce vasoconstriction which is very beneficial in conditions like **stroke**, vasospasm and hypertension.

DETD . . . and neuropeptide Y (NPY) were studied in the dog gracilis muscle in vivo. The addition of an angiotensin converting enzyme (**ACE**)-**inhibitor** and D-myoinositol-1,2,6-trisphosphate (IP.sub.3) was made in order to observe their respective effects on the above mentioned components on vasoconstrictor responses.

DETD . . . increase in blood pressure was measured directly and 2, 5 and 10 minutes after stimulation. Following the control measurements the **ACE-inhibitor** benazeprilat (10 mg i.v.) was administered. The increase in blood pressure was again measured starting 20 minutes after the administration. After these measurements, while the **ACE-inhibitor** was still in the circulation of the animal, IP.sub.3 (500 .mu.M i.v.) was administered. The increase in blood pressure was. . . monitored throughout the experiment. With this experimental set-up it was possible to obtain control data, data after distribution of the **ACE-inhibitor** per se and in combination with IP.sub. 3.

DETD The results show that the **ACE-inhibitor** reduced the norepinephrine-induced increase of blood pressure. The combined dosage with IP.sub.3 reduced also to a large extent the NPY-induced. . .

AN 94:11409 USPATFULL

TI Use of inositoltrisphosphate to treat abnormal gastrointestinal motility and secretion

IN Siren, Matti, Helsinki, Finland
Edvinsson, Lars, Lund, Sweden

PA Perstorp AB, Sweden (non-U.S. corporation)

PI US 5284839 19940208 <--
WO 9200079 19920109 <--

AI US 1993-966035 19930211 (7)
WO 1991-SE439 19910619
19930211 PCT 371 date
19930211 PCT 102(e) date

PRAI SE 1990-2278 19900628

DT Utility

EXNAM Primary Examiner: Friedman, S. J.

LREP Scully, Scott, Murphy & Presser

CLMN Number of Claims: 14

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 579

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 27 OF 41 USPATFULL

PI US 5276026 19940104 <--

DETD Additionally, the compounds of this invention are useful as therapy for **congestive heart failure**, therapy for peripheral vascular disease (e.g., Raynaud's disease), as anti-thrombotic agents, as anti-atherosclerotic agents, for treatment of cardiac hypertrophy (e.g.,. . .

DETD . . . this invention are also expected to be useful in the treatment of central nervous system vascular disorders, for example, as anti-**stroke** agents, anti-migraine agents, therapy for cerebral ischemia and therapy for subarachnoid hemorrhage, as well as in the treatment of central. . .

DETD . . . resistance, regulation of cell growth, for treatment of glaucoma, renal failure, hepatoxicity (e.g., liver cirrhosis), various endocrine hypersecretory states (e.g., **diabetes**, pheochromocytoma), drug-induced tardive diskenesia, allergies, muscular dystrophy and cancer.

DETD . . . benzthiazide as well as ethacrynic acid, tricrynafen, chlorthalidone, furosemide, musolimine, bumetanide, triamterene, amiloride and spironolactone and salts of such compounds, **angiotensin converting enzyme inhibitors** such as captopril, zofenopril, fosinopril, enalapril, delapril, pentopril, quinapril, ramipril, lisinopril, and salts of such compounds, thrombolytic agents such as. . .

AN 94:1419 USPATFULL

TI Tetrahydroethanonaphthaleneamine derivatives

IN Barrish, Joel C., Holland, PA, United States
Spergel, Steven H., Bensalem, PA, United States

PA E. R. Squibb & Sons, Inc., Princeton, NJ, United States (U.S. corporation)

PI US 5276026 19940104 <--

AI US 1993-6865 19930121 (8)

RLI Division of Ser. No. US 1990-560518, filed on 31 Jul 1990, now patented,
Pat. No. US 5202486

DT Utility

EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Gupta, Y. N.

LREP Furman, Jr., Theodore R.; Babajko, Suzanne E.

CLMN Number of Claims: 5

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1024

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 28 OF 41 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

SO Annals of Pharmacotherapy, (1994) 28/5 (617-625).
ISSN: 1060-0280 CODEN: APHRER

AB . . . to moderate hypertension, and to examine the issues surrounding the impact of these classes as well as the angiotensin-converting enzyme (**ACE**) **inhibitors**, calcium-channel blockers (CCBs), alpha-blockers, and alpha-beta-blockers on cardiovascular risk factors and cardiovascular morbidity and mortality. DATA SOURCES: A MEDLINE search. . Trials examining the impact of antihypertensive pharmacotherapy, primarily with diuretics and beta-blockers, have shown them to decrease the incidence of **stroke** by 33-50 percent. However, their effect on coronary heart disease has been disappointing, showing only a 14 .+-. 5 (mean. . . including blood pressure, plasma lipids, diabetic control/insulin sensitivity, and left ventricular hypertrophy was done. The classes included beta-blockers, diuretics, alpha-blockers, **ACE inhibitors**, and CCBs; the results show a diversity of effect. Diuretics and beta-blockers tend to worsen cardiovascular risk status, whereas the alpha-blockers. **ACE inhibitors**, and CCBs all show a beneficial effect. CONCLUSIONS: Diuretics and beta-blockers can effectively reduce cerebrovascular morbidity and mortality, but have. . .

CT Medical Descriptors:
*antihypertensive therapy
*dyslipidemia
*hypertension: DT, drug therapy
*ischemic heart disease
clinical trial
congestive heart failure
cost effectiveness analysis

diabetes control
glucose intolerance
heart infarction
heart left ventricle hypertrophy
human
hypokalemia
hypomagnesemia
incidence
insulin sensitivity
intrinsic sympathomimetic activity
lipid blood level
mortality
priority journal
review
risk factor
sex difference
stroke
*alpha adrenergic receptor blocking agent: PD, pharmacology
*alpha adrenergic receptor blocking agent: DT, drug therapy
*beta adrenergic receptor blocking agent: DT, drug. . .

AN 94145013 EMBASE
DN 1994145013
TI Hypertension: Are beta-blockers and diuretics appropriate first-line therapies?.
AU Wilson M.D.; Weart C.W.
CS Dept. of Clinical Pharmacy/Research, HealthCare Center at Christiana, 200 Hygeia Dr.,Newark, DE 19713, United States
SO Annals of Pharmacotherapy, (1994) 28/5 (617-625).
ISSN: 1060-0280 CODEN: APHRER
CY United States
DT Journal; General Review
FS 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LA English
SL English; French; Spanish

L6 ANSWER 29 OF 41 USPATFULL
PI US 5256667 19931026 <--
AB . . . ##STR1## are angiotensin II antagonists useful in the treatment of disorders related to the renin-angiotensin system (RAS) such as hypertension, **congestive heart failure**, ocular hypertension and certain CNS disorders.
SUMM . . . compounds are angiotensin II antagonists useful in the treatment of disorders related to the renin-angiotensin system such as hypertension, and **congestive heart failure**
.
SUMM . . . the regulation of normal blood pressure and seems to be critically involved in hypertension development and maintenance as well as **congestive heart failure**. Angiotension II (AII), an octapeptide hormone is produced mainly in the blood during the cleavage of angiotension I by angiotension. . .
SUMM . . . of the right eye and down the spinal column. The rats were immediately placed on a Harvard Rodent Ventilator (rate--60 **strokes** per minute, volume--1.1 cc per 100 grams body weight). The right carotid artery was ligated, both left and right vagal. . .

SUMM . . . of the invention are useful in treating hypertension. They are also of value in the management of acute and chronic **congestive heart failure** and angina. These compounds may also be expected to be useful in the treatment of primary and secondary hyperaldosteronism; renal. . . minimize the atherosclerotic process and neointimal hyperplasia following angioplasty or vascular injury and to retard the onset of type II **diabetes**. The application of

the compounds of this invention for these and similar disorders will be apparent to those skilled in. . .

SUMM . . . diltiazem, felodipine, nifedipine, amlodipine, nimodipine, isradipine, nitrendipine and verapamil; .beta.-adrenergic antagonists such as timolol, atenolol, metoprolol, propanolol, nadolol and pindolol;

angiotensin converting enzyme inhibitors such as enalapril, lisinopril, captopril, ramipril, quinapril and zofenopril; renin inhibitors such as A-69729, FK 906 and FK 744; .alpha.-adrenergic. . .

SUMM Combinations useful in the management of **congestive heart failure** include, in addition, compounds of this invention with cardiac stimulants such as dobutamine and xamoterol and phosphodiesterase inhibitors including amrinone. . .

AN 93:89674 USPATFULL

TI Quinazolinones and pyridopyrimidinones

IN Allen, Eric E., Somerset, NJ, United States
Olson, Richard E., Wilmington, DE, United States

PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)
E. I. Du Pont De Nemours & Co., Willmington, DE, United States (U.S. corporation)

PI US 5256667 19931026 <--

AI US 1992-923273 19920731 (7)

RLI Continuation-in-part of Ser. No. US 1991-765626, filed on 25 Sep 1991, now patented, Pat. No. US 5202322

DT Utility

EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Gupta, Y. N.

LREP Camara, Valeria J.; Nicholson, William J.; DiPrima, Joseph F.

CLMN Number of Claims: 7

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1575

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 30 OF 41 USPATFULL

PI US 5202486 19930413 <--

SUMM Additionally, the compounds of this invention are useful as therapy for **congestive heart failure**, therapy for peripheral vascular disease (e.g., Raynaud's disease), as anti-thrombotic agents, as anti-atherosclerotic agents, for treatment of cardiac hypertrophy (e.g.,. . .

SUMM . . . this invention are also expected to be useful in the treatment of central nervous system vascular disorders, for example, as anti-**stroke** agents, anti-migraine agents, therapy for cerebral ischemia and therapy for subarachnoid hemorrhage, as well as in the treatment of central. . .

SUMM . . . resistance, regulation of cell growth, for treatment of glaucoma, renal failure, hepatoxicity (e.g., liver cirrhosis), various endocrine hypersecretory states (e.g., **diabetes**, pheochromocytoma), drug-induced tardive diskenesia, allergies, muscular dystrophy and cancer.

SUMM . . . benzthiazide as well as ethacrynic acid, tricrynafen, chlorthalidone, furosemide, musolimine, bumetanide, triamterene, amiloride and spirono-lactone and salts of such compounds, **angiotensin converting enzyme inhibitors** such as captopril, zofenopril, fosinopril, enalapril, delapril, pentopril, quinapril, ramipril, lisinopril, and salts of such compounds, thrombolytic agents such as. . .

AN 93:29363 USPATFULL

TI Tetrahydroethanonaphthaleneamine derivatives

IN Barrish, Joel C., Holland, PA, United States
Spergel, Steven H., Bensalem, PA, United States

PA E. R. Squibb & Sons, Inc., Princeton, NJ, United States (U.S. corporation)

PI US 5202486 19930413 <--

AI US 1990-560518 19900731 (7)
DT Utility
EXNAM Primary Examiner: Robinson, Allen J.; Assistant Examiner: Kumar, Shailendra
LREP Babajko, Suzanne E.; Furman, Jr., Theodore R.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1035
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 31 OF 41 USPATFULL
PI US 5202322 19930413 <--
AB . . . ##STR1## are angiotensin II antagonists useful in the treatment of disorders related to the reninangiotensin system (RAS) such as hypertension, **congestive heart failure**, ocular hypertension and certain CNS disorders.
SUMM . . . compounds are angiotensin II antagonists useful in the treatment of disorders related to the reninangiotensin system such as hypertension, and **congestive heart failure** .
SUMM . . . the regulation of normal blood pressure and seems to be critically involved in hypertension development and maintenance as well as **congestive heart failure**. Angiotension II (AII), an octapeptide hormone is produced mainly in the blood during the cleavage of angiotension I by angiotension. . .
DETD . . . of the right eye and down the spinal column. The rats were immediately placed on a Harvard Rodent Ventilator (rate--60 **strokes** per minute, volume--1.1 cc per 100 grams body weight). The right carotid artery was ligated, both left and right vagal. . .

DETD . . . of the invention are useful in treating hypertension. They are also of value in the management of acute and chronic **congestive heart failure** and angina. These compounds may also be expected to be useful in the treatment of primary and secondary hyperaldosteronism; renal. . . minimize the atherosclerotic process and neointimal hyperplasia following angioplasty or vascular injury and to retard the onset of type II **diabetes**. The application of the compounds of this invention for these and similar disorders will be apparent to those skilled in. . .
DETD . . . diltiazem, felodipine, nifedipine, amlodipine, nimodipine, isradipine, nitrendipine and verapamil; .beta.-adrenergic antagonists such as timolol, atenolol, metoprolol, propanolol, nadolol and pindolol; **angiotensin converting enzyme inhibitors** such as enalapril, lisinopril, captopril, ramipril, quinapril and zofenopril; renin inhibitors such as A-69729, FK 906 and FK 744; .alpha.-adrenergic. . .
DETD Combinations useful in the management of **congestive heart failure** include, in addition, compounds of this invention with cardiac stimulants such as dobutamine and xamoterol and phosphodiesterase inhibitors including amrinone. . .
CLM What is claimed:
. . . nifedipine, amlodipine, rumodipine, isradapine, nitrendipine and verapamil; a .beta.-adrenergic antagonist selected from timolol, atenolol, metoprolol, propanolol, nadolol and pindolol; an **angiotensin converting enzyme inhibitor** selected from enalapril, lisinopril, captopril, ramipril, quinapril and zofenopril; a renin inhibitor selected from A-69729, FK-906 and FK-744; an .alpha.-adrenergic. . .
AN 93:29200 USPATFULL|
TI Quinazolinone and pyridopyrimidine a-II antagonists|
IN Allen, Eric E., Edison, NJ, United States
Olson, Richard E., Wilmington, DE, United States
PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

E. I. du Pont de Nemours and Company, Wilmington, DE, United States (U.S. corporation)
PI US 5202322 19930413 <--
AI US 1991-765626 19910925 (7)
DT Utility|
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Grumbling, Matthew V.|
LREP Nicholson, William H.; DiPrima, Joseph F.|
CLMN Number of Claims: 12|
ECL Exemplary Claim: 1|
DRWN No Drawings
LN.CNT 1450|
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 32 OF 41 USPATFULL
PI US 5192664 19930309 <--
WO 9011074 19901004 <--
SUMM . . . arterial blood pressure above a nominal value of 140/90 mm Hg. Diseases associated with hypertension include arteriosclerosis, hypertensive renal failure, **stroke**, **congestive heart failure** and myocardial infarction. Although numerous methods of treatment have been found to be effective in the reduction of arterial blood. . .
DETD . . . The combination is compatible with other pharmaceutical compounds used for control of hypertension and angina such as angiotensin converting enzyme (**ACE**) **inhibitors**, .beta.-adrenergic antagonists, nitrates, and diuretics.
DETD . . . been observed. PHF has been detected in the plasma of Ob/Ob mice, which are obese, hypertensive and have non-insulin dependent **diabetes**. The PHF from these mice has been isolated from the sera in the same subfraction as PHF from SHR rats. Detection of PHF may be useful in diagnosis of non-insulin dependent **diabetes** (NIDDM) and may open a new area of research into the role of PHF in NIDDM.
AN 93:18571 USPATFULL
TI Parathyroid hypertensive factor, antibodies and uses thereof
IN Pang, Peter K. T., 52225 Range Road 232, 205 Carriage Lane, Sherwood Park, Alberta, Canada T8A 245
Lewanczuk, Richard Z., Edmonton, Canada
Benishin, Christine G., Ardossen, Canada
Kaneko, Toyoii, Kanagawa, Japan
PA Pang, Peter K. T., Alberta, Canada (non-U.S. individual)
PI US 5192664 19930309 <--
WO 9011074 19901004 <--
AI US 1990-603745 19901121 (7)
WO 1990-US1577 19901121
19901121 PCT 371 date
19901121 PCT 102(e) date
RLI Continuation-in-part of Ser. No. US 1989-327450, filed on 22 Mar 1989, now abandoned And a continuation-in-part of Ser. No. US 1990-460482, filed on 3 Jan 1990
DT Utility
EXNAM Primary Examiner: Rosen, Sam
LREP Nikaido, Marmelstein, Murray & Oram
CLMN Number of Claims: 15
ECL Exemplary Claim: 1,2,4,14
DRWN 17 Drawing Figure(s); 17 Drawing Page(s)
LN.CNT 805
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 33 OF 41 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 2
SO Clinical and Experimental Hypertension, (1993) 15/6 (1205-1220). ISSN: 1064-1963 CODEN: CEHYER
AB . . . a brief synopsis of the classical antihypertensive drugs a survey
is given of the newer therapeutics, such as calcium antagonists,

ACE-inhibitors and .alpha.1-adrenoceptor antagonists. Experimental drugs, such as imidazoline receptor agonists, renin inhibitors, angiotensin II receptors antagonists, .alpha.2-adrenoceptor antagonists, potassium channel. . . the large scale of clinical evidence for a beneficial effect of long-term treatment (in particular with respect to protection against **stroke**) remains limited to diuretics and .beta.-blockers. In spite of this limitation it seems worthwhile to consider the newer antihypertensive drugs. . . the individual patient. The newer drugs may in particular offer special advantages in the presence of concomitant diseases, such as **diabetes** mellitus, hyperlipidaemia, angina pectoris or **congestive heart failure**.

AN 93344608 EMBASE
DN 1993344608
TI New avenues in antihypertensive drug treatment.
AU Van Zwieten P.A.
CS Department of Pharmacotherapy, Academic Medical Center, University of Amsterdam, Meibergdreef 15,1105 AZ Amsterdam, Netherlands
SO Clinical and Experimental Hypertension, (1993) 15/6 (1205-1220). ISSN: 1064-1963 CODEN: CEHYER
CY United States
DT Journal; Conference Article
FS 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LA English
SL English

L6 ANSWER 34 OF 41 USPATFULL
PI US 5175164 19921229 <--
SUMM . . . the regulation of normal blood pressure and seems to be critically involved in hypertension development and maintenance as well as **congestive heart failure**. Angiotensin II (A II), is an octapeptide hormone produced mainly in the blood during the cleavage of angiotensin I by. . .
SUMM . . . give compounds of the Formula I, which are angiotensin II antagonists and are useful in the treatment of hypertension and **congestive heart failure**. The compounds of the invention are useful as ocular antihypertensives.
SUMM . . . novel compounds, as the sole therapeutically active ingredient and in combination with diuretics and other antihypertensive agents, including beta blockers, **angiotensin converting enzyme inhibitors**, calcium channel blockers or a combination thereof are disclosed and claimed. Further, methods of treating hypertension and **congestive heart failure** are described and claimed.
SUMM . . . this invention are especially useful in the treatment of these conditions in patients who are also hypertensive or have a **congestive heart failure** condition.
DETD . . . of the right eye and down the spinal column. The rats were immediately placed on a Harvard Rodent Ventilator (rate--60 **strokes** per minute, volumn--1.1 cc per 100 grams body weight). The right carotid artery was ligated, both left and right vagal. . .

DETD . . . of the invention are useful in treating hypertension. They are also of value in the management of acute and chronic **congestive heart failure** and angina. These compounds may also be expected to be useful in the treatment of primary and secondary hyperaldosteronism, renal. . . process and neointimal hyperplasia following angioplasty or vascular injury and to retard the onset of the onset of type II **diabetes**. The application of the compounds of this invention for these and similar disorders will be apparent to those skilled in. . .

DETD . . . diltiazem, felodipine, nifedipine, amlodipine, nimodipine, isradipine, nitrendipine and verapamil; .beta.-adrenergic antagonists such as timolol, atenolol, metoprolol, propanolol, nadolol and pindolol;

angiotensin converting enzyme inhibitors such as enalapril, lisinopril, captopril, ramipril, quinapril and zofenopril; renin inhibitors such as A-69729, FK 906 and FK 744; .beta.-adrenergic. . .

DETD Combinations useful in the management of **congestive heart failure** include, in addition, compounds of this invention with cardiac stimulants such as dobutamine and xamoterol and phosphodiesterase inhibitors including amrinone. . .

DETD . . . of the invention are useful in treating hypertension. They are also of value in the management of acute and chronic **congestive heart failure**, in the treatment of secondary hyperaldosteronism, primary and secondary pulmonary hypertension, renal failure such as diabetic nephropathy, glomerulonephritis, scleroderma, and. . .

AN 92:106826 USPATFULL

TI Angiotensin II antagonists incorporating a substituted indole or dihydroindole

IN Bagley, Scott, Rahway, NJ, United States
Greenlee, William J., Teaneck, NJ, United States
Dhanoa, Daljit S., Tinton Falls, NJ, United States
Patchett, Arthur A., Westfield, NJ, United States

PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

PI US 5175164 19921229 <--

AI US 1991-710413 19910605 (7)

DT Utility

EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Gupta, Y. N.

LREP Camara, Valerie J.; Nicholson, William H.; DiPrima, Joseph F.

CLMN Number of Claims: 12

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 3271

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 35 OF 41 MEDLINE DUPLICATE 3

TI Management of hypertension in **diabetes**.

SO ENDOCRINOLOGY AND METABOLISM CLINICS OF NORTH AMERICA, **(1992 Jun)** 21 (2) 371-94. Ref: 146
Journal code: EMC; 8800104. ISSN: 0889-8529.

AB . . . of early and advanced diabetic nephropathy. No prospective studies have addressed the effects of antihypertensive regimens on the incidence of **congestive heart failure**, **stroke**, and coronary artery disease in large groups of diabetic patients. Such studies are urgently needed. Special consideration should be given. . . levels may become an important element in the selection an antihypertensive agent. More information, however, is needed in these areas. **ACE inhibitors**, calcium channel blockers, and alpha-adrenergic blockers probably offer a more favorable metabolic profile as compared with diuretics and beta-blockers. The. . .

CT Check Tags: Human
***Diabetes Mellitus: CO, complications**
Diabetes Mellitus: PP, physiopathology
Diabetes Mellitus, Insulin-Dependent: CO, complications
Diabetes Mellitus, Insulin-Dependent: PP, physiopathology
Diabetes Mellitus, Insulin-Dependent: TH, therapy
Diabetes Mellitus, Non-Insulin-Dependent: CO, complications
Diabetes Mellitus, Non-Insulin-Dependent: PP, physiopathology
Diabetes Mellitus, Non-Insulin-Dependent: TH, therapy
Hypertension: EP, epidemiology
Hypertension: ET, etiology
*Hypertension: TH, therapy
Insulin: BL, blood
Sodium: ME, metabolism

. . .
AN 92306954 MEDLINE
DN 92306954 PubMed ID: 1612071
TI Management of hypertension in **diabetes.**
AU Arauz-Pacheco C; Raskin P
CS Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas.
SO ENDOCRINOLOGY AND METABOLISM CLINICS OF NORTH AMERICA, **(1992 Jun)** 21 (2) 371-94. Ref: 146
Journal code: EMC; 8800104. ISSN: 0889-8529.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199207
ED Entered STN: 19920807
Last Updated on STN: 19920807
Entered Medline: 19920729

L6 ANSWER 36 OF 41 MEDLINE
SO CURRENT OPINION IN NEPHROLOGY AND HYPERTENSION, **(1992 Oct)** 1 (1) 91-9. Ref: 67
Journal code: B4H; 9303753. ISSN: 1062-4821.
AB . . . leads to the introduction of exciting new compounds. Several important clinical trials involving currently available drugs have been published recently. **Angiotensin-converting enzyme inhibitors** improved survival in patients with milder degrees of **congestive heart failure,** which indicates that they have become the cornerstone of treatment for this condition. **Angiotensin-converting enzyme inhibitors** delayed or prevented the development of diabetic proteinuria (> 200 micrograms/min) in a placebo-controlled randomized trial. Further, enalapril was more effective than metoprolol in reducing the rate of decline in renal function in patients with type I **diabetes**. Calcium channel blockers protected against acute renal failure in patients after renal transplantation in two separate studies. Calcium channel blockers. . . trial and in the Swedish Trial in Old Patients with Hypertension study (patients 65 to 85 years). In both investigations, **stroke** and cardiovascular events were significantly reduced by these conventional inexpensive agents. Clonidine was found to lower blood pressure primarily by. . .
AN 95162649 MEDLINE
DN 95162649 PubMed ID: 1365836
TI New classes of antihypertensive drugs and new findings with established agents.
AU Luft F C; Mann J F
CS University of Erlangen-Nurnberg, Germany.
SO CURRENT OPINION IN NEPHROLOGY AND HYPERTENSION, **(1992 Oct)** 1 (1) 91-9. Ref: 67
Journal code: B4H; 9303753. ISSN: 1062-4821.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199503
ED Entered STN: 19950404
Last Updated on STN: 19950404
Entered Medline: 19950323

L6 ANSWER 37 OF 41 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
SO American Journal of Cardiology, (1992) 69/13 (3E-7E).
ISSN: 0002-9149 CODEN: AJCDAG

AB Hypertension is a major risk factor for cardiovascular diseases, including
coronary artery disease (CAD), **stroke**, left ventricular hypertrophy (LVH), **congestive heart failure**, peripheral vascular disease, renal failure, and aortic aneurysms. It is also a potent promoter of atherosclerosis. Observational studies have shown a linear relationship between a wide range of blood pressures and the risk for CAD and **stroke**. Clinical trials have indicated that hypertension reduction leads to the predicted reduction in **stroke** incidence, but that CAD incidence is affected to a lesser extent than predicted. The modest effect of traditional antihypertensive drugs. . . effect on the arterial wall, which may be independent of their antihypertensive action. Beta-adrenergic blockers, calcium antagonists, and angiotensin-converting enzyme (**ACE**) **inhibitors** inhibit the development of vascular lesions in response to hypercholesterolemia or to latrogenic balloon injury, but the clinical importance of. . .

CT Medical Descriptors:
*cardiovascular disease: ET, etiology
*hypertension: DT, drug therapy
antihypertensive therapy
aorta aneurysm: CO, complication
aorta aneurysm: ET, etiology
artery intima proliferation: ET, etiology
conference paper
congestive heart failure: ET, etiology
coronary artery disease: ET, etiology
diabetes mellitus
drug mechanism
heart left ventricle hypertrophy: ET, etiology
heart left ventricle mass
heart muscle perfusion
human
hypercholesterolemia
incidence
kidney failure: ET, etiology
kidney function
peripheral vascular disease: ET, etiology
priority journal
stroke: ET, etiology
*beta adrenergic receptor blocking agent: DT, drug therapy
*beta adrenergic receptor blocking agent: PD, pharmacology
*calcium antagonist: DT, drug therapy
*calcium. . .

AN 92164983 EMBASE
DN 1992164983
TI Vascular effects of systemic hypertension.
AU Chobanian A.V.
CS Whitaker Cardiovascular Institute, Boston University School of Medicine, 80 East Concord Street,Boston, MA 02118, United States
SO American Journal of Cardiology, (1992) 69/13 (3E-7E).
ISSN: 0002-9149 CODEN: AJCDAG
CY United States
DT Journal; Conference Article
FS 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LA English
SL English

L6 ANSWER 38 OF 41 USPATFULL
PI US 5070088 19911203 <--
DETD Additionally, the compounds of this invention are useful as therapy for **congestive heart failure**, therapy for peripheral vascular disease (e.g., Raynaud's disease), as anti-thrombotic agents, as anti-atherosclerotic agents, for treatment of

cardiac hypertrophy (e.g.,. . .

DETD . . . this invention are also expected to be useful in the treatment of central nervous system vascular disorders, for example, as anti-**stroke** agents, anti-migraine agents, therapy for cerebral ischemia and therapy for subarachnoid hemorrhage, as well as in the treatment of central. . .

DETD . . . resistance, regulation of cell growth, for treatment of glaucoma, renal failure, hepatoxicity (e.g., liver cirrhosis), various endocrine hypersecretory states (e.g., **diabetes**, pheochromocytoma), drug-induced tardive dyskenesia, allergies, muscular dystrophy and cancer.

DETD . . . benzthiazide as well as ethacrynic acid, tricrynafen, chlorthalidone, furosemide, musolimine, bumetanide, triamterene, amiloride and spironolactone and salts of such compounds, **angiotensin converting enzyme inhibitors** such as captopril, zofenopril, fosinopril, enalapril, delapril, pentopril, quinapril, ramipril, lisinopril, and salts of such compounds, thrombolytic agents such as. . .

AN 91:98391 USPATFULL

TI Pyranyl quinoline calcium channel blockers

IN Atwal, Karnail, Newtown, PA, United States

PA E. R. Squibb & Sons, Inc., Princeton, NJ, United States (U.S. corporation)

PI US 5070088 19911203 <--

AI US 1989-452999 19891219 (7)

DT Utility

EXNAM Primary Examiner: Rotman, Alan L.

LREP Furman, Jr., Theodore R.; Babajko, Suzanne E.

CLMN Number of Claims: 20

ECL Exemplary Claim: 1,20

DRWN No Drawings

LN.CNT 544

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 39 OF 41 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

SO American Journal of Hypertension, (1991) 4/7 II SUPPL. (494S-502S). ISSN: 0895-7061 CODEN: AJHYE6

AB . . . efficacy has been tested in many trials. An outstanding result of these trials has been their clear success in preventing **stroke** and **stroke**-related deaths and in decreasing the incidence of **congestive heart failure** (CHF) and renal disease. A similar success has not been achieved in reducing coronary heart disease endpoints. Diuretics and .beta.-blockers. . . their role in hypertension and its sequelae. Other classes of antihypertensive drugs such as the calcium antagonists, angiotensin converting enzyme (**ACE**) **inhibitors**, and .alpha.1-antagonists do not share these adverse effects. It has become increasingly clear tht effective antihypertensive therapy includes both the. . .

CT Medical Descriptors:
*cardiovascular system
***diabetes mellitus**
*hyperinsulinemia
*hyperlipidemia
*hypertension: DT, drug therapy
conference paper
human
*beta adrenergic receptor blocking agent: DT, drug therapy
*calcium channel blocking agent: DT, drug therapy
*thiazide diuretic. . .

AN 91230906 EMBASE

DN 1991230906

TI Metabolic consequences of treating hypertension.

AU Pool P.E.; Seagren S.C.; Salel A.F.

CS North County Cardiology Research Laboratory, 1087 Devonshire Dr., #300, Encinitas, CA 92024, United States

SO American Journal of Hypertension, (1991) 4/7 II SUPPL. (494S-502S).
ISSN: 0895-7061 CODEN: AJHYE6
CY United States
DT Journal; Conference Article
FS 003 Endocrinology
006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
LA English
SL English

L6 ANSWER 40 OF 41 USPATFULL
PI US 4902684 19900220 <--
SUMM Additionally, the compounds of this invention are useful as therapy for **congestive heart failure**, therapy for peripheral vascular disease (e.g., Raynaud's disease), as anti-thrombotic agents, as anti-atherosclerotic agents, for treatment of cardiac hypertrophy (e.g.,. . .
SUMM . . . this invention are also expected to be useful in the treatment of central nervous system vascular disorders, for example, as anti-**stroke** agents, anti-migraine agents, therapy for cerebral ischemia and therapy for subarachnoid hemorrhage, as well as in the treatment of central. . .
SUMM . . . resistance, regulation of cell growth, for treatment of glaucoma, renal failure, hepatoxicity (e.g., liver cirrhosis), various endocrine hypersecretory states (e.g., **diabetes**, pheochromocytoma), drug-induced tardive dyskenesia, allergies, muscular dystrophy and cancer.
SUMM . . . benzthiazide as well as ethacrynic acid, tricrynafen, chlorthalidone, furosemide, musolimine, bumetanide, triamterene, amiloride and spironolactone and salts of such compounds, **angiotensin converting enzyme inhibitors** such as captopril, zofenopril, fosinopril, enalapril, delapril, pentopril, quinapril, ramipril, lisinopril, and salts of such compounds, thrombolytic agents such as. . .
AN 90:13419 USPATFULL
TI Benzazepine and benzothiazepine derivatives
IN Floyd, David M., Pennington, NJ, United States
Hunt, John T., Princeton, NJ, United States
Kimball, Spencer D., East Windsor, NJ, United States
Krapcho, John, Somerset, NJ, United States
Das, Jagabandhu, Hamilton Square, NJ, United States
Rovnyak, George C., Hopewell, NJ, United States
Barrish, Joel C., Holland, PA, United States
PA E. R. Squibb & Sons, Inc., Princeton, NJ, United States (U.S. corporation)
PI US 4902684 19900220 <--
AI US 1989-353806 19890522 (7)
RLI Continuation-in-part of Ser. No. US 1988-208521, filed on 20 Jun 1988, now abandoned
DT Utility
EXNAM Primary Examiner: Bond, Robert T.
LREP Furman Jr., Theodore R.
CLMN Number of Claims: 43
ECL Exemplary Claim: 1,42
DRWN No Drawings
LN.CNT 3839
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 41 OF 41 MEDLINE
SO AMERICAN JOURNAL OF MEDICINE, **(1988 Apr 15)** 84 (4A) 24-9.
Journal code: 3JU; 0267200. ISSN: 0002-9343.
AB Reduction of elevated blood pressure is effective in reducing morbidity and mortality from cardiovascular disease in general. Striking decreases in **stroke, congestive heart failure**

, and renal impairment have been observed when blood pressure is reduced. However, the ability of traditional, diuretic-first, stepped-care therapeutic algorithms. . .

CT Check Tags: Human
Adrenergic beta-Antagonists: TU, therapeutic use
Angiotensin-Converting Enzyme Inhibitors: TU, therapeutic use
*Cardiovascular Diseases: ET, etiology
Cardiovascular Diseases: PP, physiopathology
Diabetes Mellitus: CO, complications
Diuretics, Thiazide: TU, therapeutic use
Hypertension: BL, blood
Hypertension: CO, complications
*Hypertension: DT, drug therapy
Hypertension:. . .

CN 0 (Adrenergic beta-Antagonists); 0 (**Angiotensin-Converting Enzyme Inhibitors**); 0 (Diuretics, Thiazide); 0 (Lipids)

AN 89116207 MEDLINE

DN 89116207 PubMed ID: 2905869

TI Cardiovascular risk factors and antihypertensive therapy.

AU Weinberger M H

CS Hypertension Research Center, Indiana University School of Medicine, Indianapolis 46223.

SO AMERICAN JOURNAL OF MEDICINE, **(1988 Apr 15)** 84 (4A) 24-9.
Journal code: 3JU; 0267200. ISSN: 0002-9343.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 198903

ED Entered STN: 19900308
Last Updated on STN: 19950206
Entered Medline: 19890302

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(FILE 'HOME' ENTERED AT 16:41:51 ON 07 JUN 2001)

FILE 'EMBASE, MEDLINE, CAPLUS, BIOSIS, USPATFULL' ENTERED AT 16:42:19 ON 07 JUN 2001

L1 53318 S ACE INHIBITOR OR ANGIOTENSIN CONVERTING ENZYME INHIBITOR
L2 845983 S CONGESTIVE HEART FAILURE OR DIABETES OR STROKE
L3 11384 S L1 AND L2
L4 7148 S L3 AND PY<1998
L5 48 S L4 AND DIABETES AND STROKE AND CONGESTIVE HEART FAILURE
L6 41 DUP REM L5 (7 DUPLICATES REMOVED)